PREVALENCE OF THYROID DYSFUNTION IN ADULT HIV PATIENTS ON HIGHLY ACTIVE ANTI RETROVIRAL THERAPY IRRESPECTIVE OF STAGING AND CORRELATION BETWEEN TSH AND CD4 COUNT

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CERTIFICATE

This is to certify that the dissertation titled **"Prevalence of Thyroid Dysfunction in Adult HIV Patients on Highly Active Anti Retroviral Therapy Irrespective of Staging And Correlation Between TSH and CD4 Count"** is the bonafide original work of Dr.P.Karthik in partial fulfillment of the requirements for M.D. Branch – I (General Medicine) Examination of the Tamil nadu Dr.M.G.R Medical University to be held in September 2014. The Period of study was from April 2014 to September 2014.

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DECLARATION

I, Dr.Karthik.P solemnly declare that dissertation titled **"Prevalence of Thyroid Dysfunction in Adult HIV Patients on Highly Active Anti Retroviral Therapy Irrespective of Staging And Correlation Between TSH and CD4 Count"** is a bonafide work done by me at Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai-3 during April 2014 to September 2014 under the guidance and supervision of my unit chief PROF. S. RAJASEKARAN, M.D., Professor of Medicine, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai.

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PREVALENCE OF THYROID DYSFUNCTION IN ADULT HIV PATIENTS ON HAART IRRESPECTIVE OF STAGING AND CORRELATION BETWEEN THE TSH AND CD-4 COUNT

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ABSTRACT

OBJECTIVE:

This study was done to know the prevalence of thyroid dysfunction in adult HIV patients on HAART irrespective of staging and correlation between the TSH and CD-4 count.

METHODOLOGY:

Patient attending ART centre in madras medical college in RGGGH are included in the study. Questionnaire and clinical examination was done and free T3, T4, TSH and CD-4 count was done. Sample size is 100. Study period is 6 months APRIL – 2014 to SEPTEMBER – 2014.

RESULTS:

The prevalence of thyroid dysfunction in our study is 11% (11 out of 100 patients). Overt hypothyroidism – 2%, subclinical hypothyroidism – 9%. 8 patients are male sex and CD-4 count less than 200. There is significant negative correlation between CD-4 count and TSH (Pearson Chi-Square *p* value .000).

CONCLUSION:

There is increased prevalence of thyroid dysfunction in HIV patients on HAART especially male sex, low CD-4 count and longer duration of disease.

KEY WORDS: *HIV, HAART, TSH, CD-4*

INTRODUCTION

HIV [human immuno deficiency virus] the etiological agent of AIDS. Two types HIV virus HIV 1 and HIV 2 which causes cytopathic effects either directly or indirectly .

The various spectrum of endocrine dysfunctions manifested in patients with HIV are related directly to virus or secondary to opportunistic infections, drugs, malignancy and mainly affects ADRENAL GLAND, GONADS, THYROID, PITUTARY.

Thyroid Dysfunction is a recognized entity in HIV infection.

Thyroid function alteration seen in up to 10 to 15% of HIV patients.

The predominant abnormality is sub clinical hypothyroidism but both overt hypothyroidism and hyperthyroidism may occur in HIV infected patients.

PATTERN OF THYROID ABNORMALITY IN HIV PATIENTS

Sub clinical hypothyroidism

Overt hypothyroidism

Hyperthyroidism [subclinical / overt]

Immune reconstitution Graves disease.

The dysfunctions may caused by direct effects of HIV on thyroid gland or due to opportunistic infections that occurs in HIV patients, or neoplasm .

The risk factor for development of thyroid dysfunctions in HIV patients are

- Low CD4 count
- Male sex
- Longer duration of disease
- HAART.
- Advanced disease

In the setting of HAART , up to 10% of patients have elevated TSH may a manifestations of immune reconstitution .

Immune reconstitution grave s disease may be occur as a late complication of HAART.

The various studies shows that TSH level negatively correlates with CD4 count, and abnormalities in thyroid function may used as surrogate marker of advancing HIV infection in infected adults.

In this study 100 HIV infected adult patients, aged above 18 years are studied about symptoms related to thyroid dysfunctions and TFT and CD4 count measured .

The prevalence of thyroid dysfunction and correlation between TSH and CD4 count analyzed.

It is important to evaluate thyroid function in HIV patients because various studies shows a higher than expected incidence of overt hypothyroidism found in patient receive HAART.

Recommends universal screening of thyroid function in HIV patients on HAART especially in symptomatic and patients with risk factor for developing thyroid dysfunction.

AIMS AND OBJECTIVES

The study was done to know the prevalence of thyroid dysfunction in adult hiv patients on highly active anti retro viral therapy irrespective of stage of disease and find out the correlation between TSH level and CD4 count.

REVIEW OF LITERATURE

HISTORY [1]

HIV belongs to family Retrovirus and sub family Lenti virus. HIV was first recognized at USA among homosexual men on 1981 and the virus was first isolated from patients with lymphadenopathy in 1983. The initial reporting manifestations were P.jiroveci pneumonia and Kaposi's sarcoma. It has spread all over the world. HIV is the causative agent of AIDS and demonstrated at 1984. In 1985 the sensitive Diagnostic method ELISA developed. HIV infection was first detected in India in 1986, among female sex workers in Chennai. NACO launched the Highly Active Anti Retroviral Therapy (HAART), in the form of fixed drug combinations on April 2004.[2] The most common mode of spread is heterosexual.

Global summary of the AIDS epidemics as on December 2012 [3]

Number of people living With HIV at the end of 2012

- Total 35.3 million (32.2 - 38.8 million
- Women 17.7 million (16.4 – 19.3.million)

People newly infected with HIV at the end of 2012

- Total 2.3 million (1.9 – 2.7 million)

AIDS deaths at the end of 2012

- Total 1.6 million (1.4 – 1.9 million

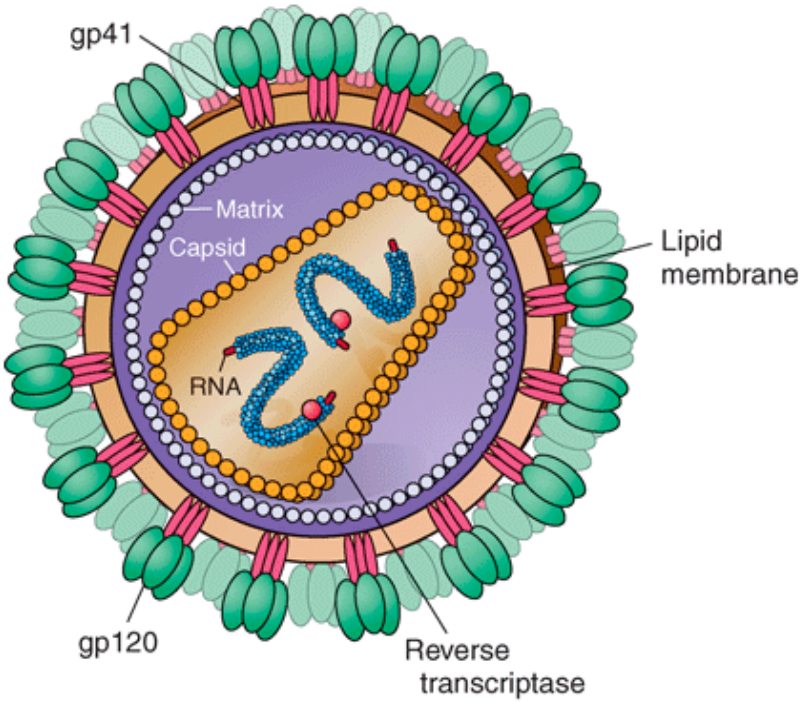
The sub Saharan Africa remains the most severly affected in worldwide, approximately 1 in every 20 adults living with hiv. And accounts for 71% of HIV infection patients worldwide.

IN INDIA[4]

Number of people living with HIV in india – 2.4 million [1.93 – 3.04].

Male	-	61%
Female	-	39%
Children < 14 yrs	-	4.4%
Age 15 – 49 yrs	-	82.4%
Over 50 yrs	-	13.2%

STRUCTURE OF HIV-1



"The gp120 envelope, gp41 transmembrane components of the envelope, genomic RNA, enzymereverse transcriptase, p18(17) inner membrane (matrix), and p24 core protein (capsid)"

ETIOLOGIC AGENT

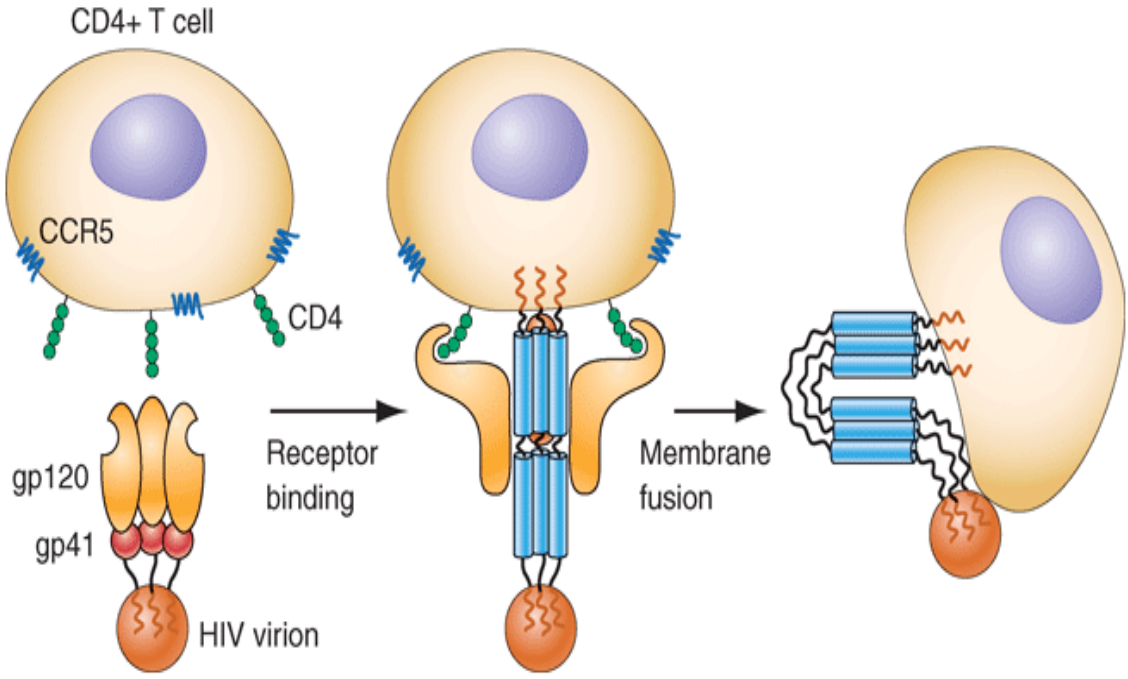
HIV-1 and HIV-2 both cause cytopathic effects either directly or indirectly ..

HIV-1 is the most common cause in world wide..

HIV-2 first identified in 1986 and originally confined to west Africa.

Currently defined groups of HIV- 1 [M, N, O, P] , HIV - 2 [A through G], each likely derived from a separate transfer to humans from non human primates.

Binding and fusion of HIV-1 with its target cell



"HIV-1 binds to its target cell via the CD4 molecule, leading to a conformational change in the gp120 molecule that allows it to bind to the co-receptor CCR5 (for R5-using viruses). The virus then firmly attaches to the host cell membrane in a coiled-spring fashion via the newly exposed gp41 molecule. Virus-cell fusion occurs as the transitional intermediate of gp41 undergoes further changes to form a hairpin structure that draws the two membranes into close proximity"

MORPHOLOGY OF HIV[5, 6]

From the antigenic point of view, we can group HIV structure into:

Envelop

Main component for binding to CD4+ T cells.

Principal antigens are – gp41, gp120.

Nucleocapsid consists of:

Outer icosahedral shell – Principal antigen is p18 (shell antigen).

Inner cone shaped core – core antigens – p24 (principal antigen) Other – P15, P35.

RNA

Constitutes the genome

Polymerase antigens – p31, p51, p66

HIV Genome

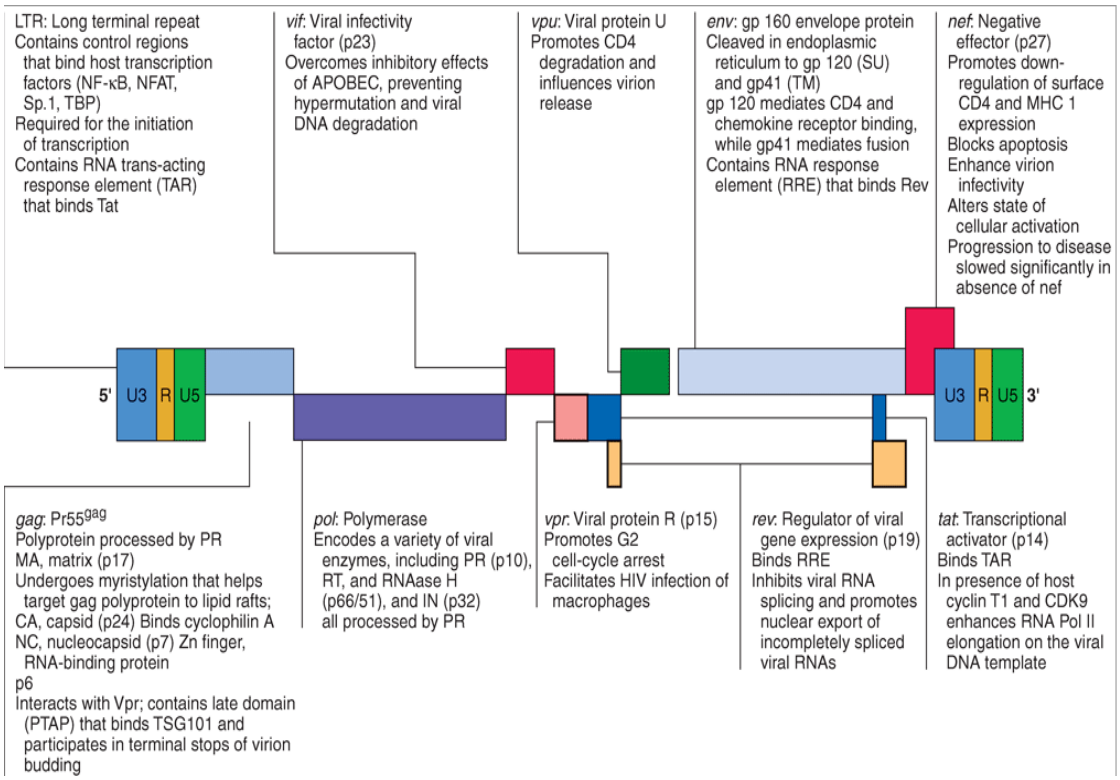


Figure-3 illustrates schematically the arrangement of the HIV genome. The major difference between the genomes of HIV-1 and HIV-2 is the fact that HIV-2 lacks the vpu gene and has a vpx gene not contained in HIV-1

VIRAL GENOME

The genome contains the three structural genes and other nonstructural genes and regulatory genes specific for virus.

The products of structural and nonstructural genes acts as antigens, sera of infected persons have antibodies to them and detection of these antigen and antibodies useful in diagnosis and prognosis of HIV infection.

STRUCTURAL GENES

1.GAG genes-determine the core and shell of the virus .It Expressed as a precursor protein P 55 cleaved into three proteins which make up viral core and shell. [P15, P18, P24].

The major core antigen is P24 ,it can be detected in early stage of HIV infection before antibodies to appear.

2. ENV – synthesis of envelope GP 160 which cleaved into gp120 the surface spike protein ,and gp41 a transmembrane anchoring protein.

Antibodies to gp 120are present in circulation till the terminal stage of infection.

3.PLO gene – codes for polymerase reverse transcriptase and other viral enzyme.

HIV REPLICATION

- The replication cycle begins with binding of gp120 via V1 region near N terminus to its receptor on host cell surface, the CD4 molecule.

- The CD4 molecule is a 55kDa protein found in predominantly helper T lymphocytes, and also expressed in monocytes , macrophage, dentritic cell, langerhans cell..

- Once gp120 binds to CD4, the gp120 undergoes conformational changes which facilitates binding to major co-receptor.

- Following conformational changes gp120 fusion with host cell membrane via gp41 molecule penetrates the plasma membrane of target cell..

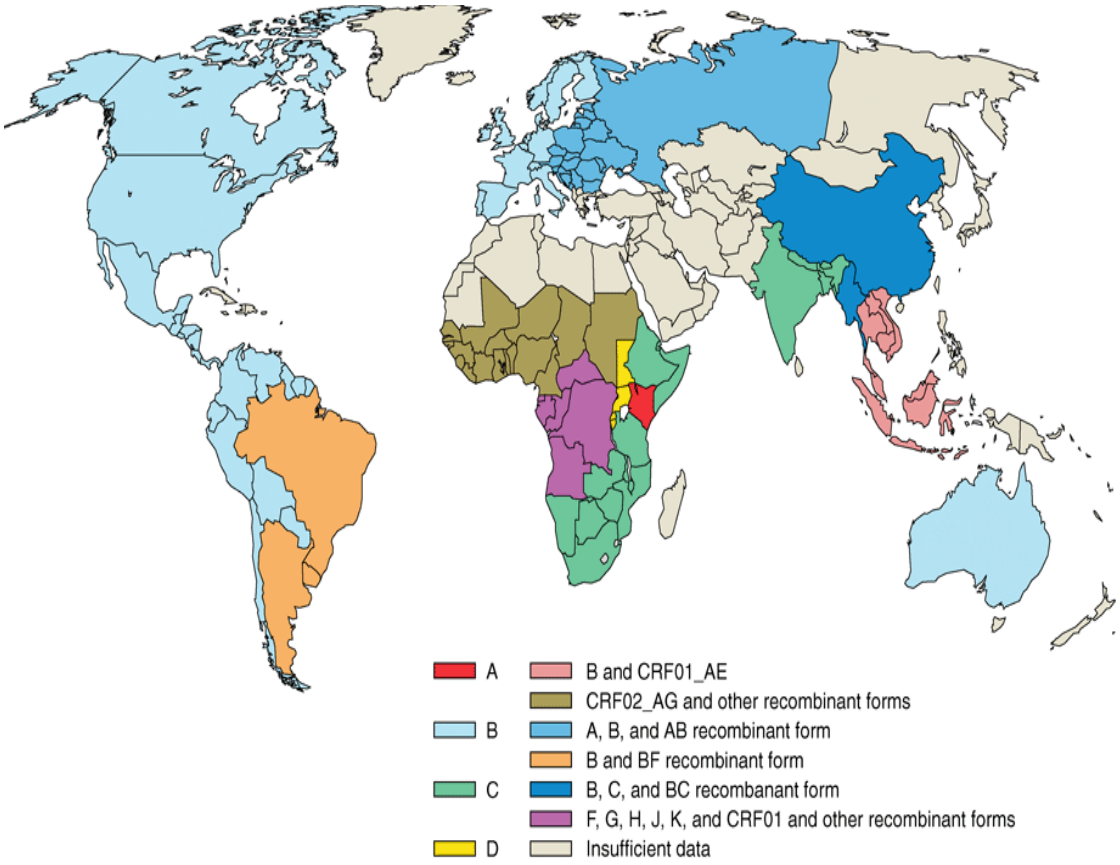
- Then coiling upon itself to bring the virion and target cell together leads to formation of preintegration complex , composed of viral RNA and viral enzymes, surrounded by a capsid protein coat , is released into cytoplasm of cell.

- The viral reverse transcriptase enzyme catalyzes the genomic RNA into DNA and protein coat opens to release the resulting double standard proviral HIV DNA.

- Activation of cell - The viral DNA integrated to the host cell chromosomes through integrase enzyme..and HIV proviral DNA integrates into nuclear DNA preferentially within introns of active genes and regional hot spots.

❖ The provirus may remain transcriptionally inactive [latent] or may manifest varying level of gene expression up to active production of virus..

GLOBAL VARIATIONS OF HIV-1



Geographic distribution of HIV-1 subtypes and recombinant forms

ORIGIN OF THE HIV EPIDEMIC

Molecular phylogenetic studies suggest that HIV evolved from simian immunodeficiency virus (SIV), which has been found

in two of four subspecies of chimpanzees in the Cameroon[7]. HIV has evolved into groups M, N and O; M ("Main") is considered the pandemic strain and comprises the vast majority of strains of HIV. Viruses from group M are subsequently divided into ten distinct subtypes (A to J). Group O ("Outlier") represents far fewer strains from Cameroon, Gabon and Equatorial Guinea. Group N ("non-M / non-O") is represented by very few isolates and has only been documented in Cameroon. Studies have been performed to ascertain the origins of HIV infection. Through sequence analysis, the origins of pandemic (group M) and nonpandemic (group N) HIV could be traced to isolate geographically chimpanzee communities[8]. The origin of group O HIV is still unknown.

CASE DEFINITION - INDIA (ABOVE 12 YEARS OF AGE)

1) Two positive tests for HIV infection by ERS test (Elisa/Rapid/Simple) AND

2) Any one -criteria
   a. Significant weight loss (>10% of body weight) within last 1 month/cachexia (rather than HIV infection). AND Chronic diarrhea (intermittent or continuous) >one month duration or prolonged fever (intermittent or continuous) >one month duration.

b. Tuberculosis: Extensive pulmonary, disseminated, milliary, extra-pulmonary tuberculosis.

c. Neurological impairment preventing independent daily activities, not known to be due to the conditions unrelated to HIV infection (e.g. trauma)

d. Candidiasis of the oesophagus (diagnosable by oral candidiasis by odynophagia)

e. Clinically diagnosed life threatening or multiple episodes of pneumonia, with or without etiological confirmation.

f. Kaposi Sarcoma

g. Other conditions:

   i. Cryptococcal meningitis

   ii. Neuro Toxoplasmosis

   iii. CMV retinitis

   iv. P.marneffei

   v. Recurrent Herpes Zoster or multi-dermatomal herpes infection

   vi. Disseminated molluscum

DEFINITION

"The CDC classification system This system is based on:

1) Clinical conditions of HIV infection

2) CD4+ count

Confirmed by Elisa and Western blot with CD4+ count <200/mm^3 And / or

Category-A

- Asymptomatic HIV infection
- Persistent generalized lymphadenopathy
- Acute (Primary) HIV infection with accompanying illness or history of acute HIV infection.

Category-B

Consists of symptomatic conditions in an HIV-infected adolescent or adult that are not included among conditions listed in clinical category C and meet at least one of the following criteria:

1) The conditions are attributed to HIV infection or are of a defect in cell-mediated immunity; or

2) The conditions are considered by physicians to have a clinical course or to require management and complicated by HIV infection. Examples

a. Bacilliary angiomatosis

b. Candidiasis, oropharyngeal (thrush)

c. Candidiasis, vulvovaginal; persistent, frequent, or poorly response to therapy.

d. Cervical dysplasia (moderate or severe) /cervical carcinoma in situ.

e. Constitutional symptoms, such as diarrhea lasting >1month or fever (38.5°C) .

f. Hairy leukoplakia,

g. Herpes zoster (shingles), involving at least two distinct pisodes or more than one dermatome.

h. Idiopathic thrombocytopenic purpura

i. Listeriosis

j. Pelvic inflammatory disease, if complicated by tuboovarian abscess.

k. Peripheral neuropathy

CATEGORY C CONDITION

1) Candidiasis of bronchi, trachea, lungs or esophagus

2) Cervical cancer invasive

3) Coccidioidomycosis disseminated or extra pulmonary

4) Extra pulmonary Cryptococcosis ,

5) Cryptosportidiosis- intestinal (>1 month)

6) Cytomegalovirus disease other than spleen, liver, or node

7) HIV encephalopathy

8) Herpes simplex, chronic (>1 month), or bronchitis, pneumonia, or esophagitis.

9) Histoplasmosis, disseminated or extra pulmonary

10) Isosporiasis - intestinal (>1 month)

11) Kaposi sarcoma

12) Lymphoma (Burkitt's primary CNS)

13) MAC disseminated or extra pulmonary

14) M. tuberculosis - any site

15) Pneumocystis carinii pneumonia

16) Pneumonia- recurrent

17) Progressive multifocal leukoencephalopathy

18) Salmonella septicaemiae, recurrent

19) Toxoplasmosis- brain

20) Wasting syndrome - HIV

21) Any HIV infected individual with CD+ T cell count <200/µl has AIDS by definition, irrespective of the presence of symptoms or opportunistic disease".

WHO CLINICAL STAGING OF HIV/AIDS FOR ADULTS AND ADOLESCENTS

Developed by WHO in 1990 and revised in 2007.

Based on clinical findings, that guides diagnosis , evaluation, and management and does not require CD4 count.

Used in many countries to determine eligibility for antiretro viral therapy.

Categorized as 1 to 4 stages , progressing from primary HIV infection to advanced HIV/AIDS.

PRIMARY HIV INFECTION

Asymptomatic

Acute retroviral syndrome

CLINICAL STAGE I

Asymtomatic

Persistent generalized lymadenopathy

CLINICAL STAGE 2

Moderate unexplained weight loss [< 10% of presumed or measured body weight]

Recurrent respiratory tract infection

Herpes zoster

Angular cheilitis

Recurrent oral ulceration

Papular pruritic eruptions

Seborrheic dermatitis

Fungal nail infection

CLINICAL STAGE 3

Unexplained severe weight loss [> 10% of presumed or measured body weight]

Unexplained chronic diarrhea for more than one month

Unexplained persistent fever >37.6*C intermittent or constant, for more than one month

Persistent oral candidiasis

Oral hairy leukoplakia

Pulmonary tuberculosis

Acute necrotizing ulcerative stomatitis

Chronic thrombocytopenia

Unexplained anemia

CLINICAL STAGE 4

Pnemocysti pneumonia

HIV wasting syndrome

Recurrent severe bacterial pneumonia

Chronic herpes simplex infection

Esophageal candidiasis

Extra pulmonary tb

Kaposi sarcoma

CMV infection

Cns toxoplasmosis

MAC infection

Disseminated mycosis

Lymphomas

Chronic cryptosporidiosis

HIV associated nephropathy/cardiomyopathy.

MODES OF TRANSMISSION AND DYNAMICS[9]

Sexual Transmission

- Sexual transmission- via hetero and homosexual contact.
- Parenteral transmission: among injection drug users (IDU), blood transfusions.
- Perinatal transmission.

FACTORS INFLUENCE THE SEXUAL TRANSMISSION

Presence of other STDs

- Strongly associated with HIV transmission
- Genial infections are linked to increased risk of hiv via sexual transmission. e.g., Treponema pallidum, Haemophilus ducreyi and herpes simplex virus.
- The non ulcerative inflammatory genital infections like C.trachomatis, N.gonorrhoea, T.vaginalis also increase the risk of transmission.

Level of Plasma Viremia:

- The main factor that determines the heterosexual transmission is level of plasma viremia.
- Transmission is rare when viral load in plasma less than 1700 copies of HIV RNA per ml. Level of HIV RNA was highest at early phase of infection .

Male Circumcision

- It has lower risk of HIV infection.
- In uncircumcised men there is increased susceptibility of ulcerative STDs, and a high density of langerghans CD4 cells in highly vascularised inner foreskin.

Alcohol and illicit drug use

- Its usage increases the risk of HIV transmission via unsafe sexual behaviors, both homosexual and heterosexual.

TRANSMISSION BY BLOOD AND BLOOD PRODUCTS[10, 11]

Blood Product.

The blood products that Capable of transmitting HIV transmission are

- Whole blood, packed RBC's, Platelets
- Leukocytes, plasma concentrates of clotting vaccine

Not associated with HIV.

While processing these products the viral elements are inactivated or removed.

- Hyperimmune gamma globulin
- HB immune globulin, plasma derived
- Plasma derived hep B
- Rho immune globulin.

There is no reported case of HIV- 2 transmission via donated blood or tissues in united states.

TRANSMISSION IN I .V. DRUG USER [10,11]

Occupational transmission:

Transmission through intact skin has not been documented.

Transmission to health care worker and laboratory from a health care personal who work with HIV-containing few materials.

Transmission of infection worker to patients.

Potential place of health care workers to get HIV infection

Sl. No.	Exposure	Risk
1.	Needle stick injuries cut by sharp object	0.3%
2.	Contact with blood, tissue or other body fluid	0.09%
3.	Contact of non intact skin is less risk than mucous membrane	

Factors associated with increased risk for HIV infection

- Percutaneous exposure – high risk
- Blood level:
- Device visibly contaminated with patients blood
- Needle placed directly in a vein or artery
- Deep injury

Mucocutaneous exposure:

- Exposure of high volume blood
- Prolonged period of contact
- Portal entry

Exposure to blood of advanced stage disease patients

- High level titre of HIV in blood
- More virulent strains of virus

HIV containing material – different body fluids have different potential for HIV transmission. they can be classified as:

Highest risk	**Fluids considered potentially infectious (but risk much lower than blood exposure and not commonly implicated in occupational exposure)**	**Fluid not considered potentially infectious unless visibly bloody**
Blood and visible bloody body fluids	CSF, synovial-fluid, pleural fluid, peritoneal fluid, pericardial fluid, amniotic fluid	Feces, nasal secretions, saliva sputum, sweat, tears, urine, vomitus

FETAL / INFANT TRANSMISSION

HIV transmission from an infected mother to her fetus can occur at various stage

During pregnancy	**Perinatal period**	**Breast feeding**
23 – 30% of cases	Most common period (50 – 60%)	2 – 20%
Can occur as early as 1st and 2nd trimester		

Overall, probability of transmission (HIVfrom mother to fetus (in absence of prophylactic ART) is 15 – 25% in industrialized countries and 25 – 35% in developing countries.

Factors associated with higher rates of transmission

High maternal levels of plasma viremia

The risk increases steadily as the level of maternal plasma viremia increases.

There is no cutoff value below that transmission never occurs.

Low maternal CD4+ T cell count

It is correlated with high levels of plasma viremia.

Closer HLA – match between mother and child.

- Factor important for transmission during labour or perinatal period is Prolonged interval between membrane rupture and delivery.
- Factors associated with increased mother to child transmission via breast feeding.
- Mastitis
- Low level of maternal CD4+ T cell counts

- Low level of vitamin A .
- Breast feeding during early month
- Mixed feeding – higher risk than exclusive breast feeding.

GUIDELINES FOR DECREASING MATERNAL-FETAL TRANSMISSION

Use of ART

For mother who requires therapy for her HIV infection	For mother who does not need treatment to HIV infection
Combined treatment for mother during pregnancy through delivery + Prophylaxis for infant	Antiretroviral prophylaxis with one or more drugs + Prophylaxis for infant

In developing countries, if about regimens cannot be used, short course prophylactic ARV regimens can be used.

OBSTETRIC MANAGEMENT

- Combination ARV combined with cesarean section delivery, significantly decreases risk of maternal – fetal transmission.
- Breast Feeding
  - In developed countries – avoidance of breast feeding by infected mother.

- Developing countries, the optimal approach is to provide continual treatment to infected mother who breast feed their infant. Also, intermittent administrative of nevirapine to the uninfected babies is being tried.

Mode	Risk of transmission	Number of cases
Sexual route	0.01 – 1.0%	>80%
Mother to child route	30	1%
Blood products	90	3 – 5%
Infected syringes and needles – IDU	0.5 – 1.0	– 10%

WINDOW PERIOD

Antibody detection - 22 days

P24 Ag detection - 16 days

Nucleic acid testing - 12 days

ELISA – STANDARD BLOOD SCREENING TEST FOR HIV INFECTION

- Usually detects both HIV – 1 and HIV – 2
- Sensitivity >99.5%; Specificity – not optional

- From positive Elisa to a negative Elisa on treatment does not indicate clearing of infection; it signifies levels of ongoing exposures to virus insufficient to maintain a measurable antibody response.

WESTERN BLOT – (HIGHLY SPECIFIC)

- Positive western blot – FDA criteria (1993) – Antibodies to 2 of the 3 HIV proteins; p24, gp41 and gp 120/160.
- Antibody band to polgene product p31 should also be checked to rule out false positive.
- Negative western bolt – is one in which no bands are present at molecular weights corresponding to HIV gene products.
- Causes – early HIV-1, HIV-2, pregnancy, antibodies that cross react with proteins of HIV ego antibodies that react with p24 and/or p55.

For indeterminate cases:

- Repeat western blot after 1 month
- Attempt to confirm a diagnosis of HIV with:
  - P24 antigen capture assay
  - One of the tests for HIV RNA

P24 ANTIGEN CAPTURE ASSAY

- Elisa or EIA – type assay
- Positive in maximum up to 50% patients.
- Greatest use – screening test for HIV infection during suspected acute HIV syndrome.

HIV – RNA TESTING

Very useful in settings where anti – HIV antibodies may be misleading.

1. Acute infection
2. Neonatal infection

Methods	Principle	Sensitivity
RT – PCR	Target amplification	Reliable to 40 copies/ml of HIVRNA
B DNA	Signal amplification	Reliable to 50 copies/ml of HIVRNA

LAB MONITORING OF PATIENTS WITH HIV INFECTION

CD4+ T cell counts

- Correct measure of immunologic competence to HIV infected patients.
- Measurement made either

- Directly
- Percent of CD4+ T cells and total lymphocyte count.

- To Test the infection- during the time of diagnosis and evry 3 -6 months.

- Practical use of CD4+ T cell count:
  - If CD4+ Tee count <350/ml – indication for initiating ART therapy.
  - Decline in CD4+ T cell count >25% - indication of change the therapy.

- CD4+ count is <200/ml – start regimen for p.jiroveci prophylaxis

- If count <50/ml – start primary prophylaxis for MAC

HIV RNA DETERMINATIONS

- To Measure the change in HIV RNA levels useful for
  - Assessing rate of disease progression
  - viral turnover

- Correlation between immune system activation and viral replication.
- To assess the occurrence of drug resistance

- Decisions based upon HIV RNA level should never be made on a single determination, because of fluctuation during the secondary infections or immunization.

- To measure HIV RNA levels during at the time of diagnosis and every 3 – 6 months for whom are all not taking ART.

TEST OF HIV RESISTANCE

- Done through – genotypic assays and phenotypic assays

- They enhance short term ability to decrease viral load by 0.5 log compared simply on changing drugs .

- Useful for: to Select the new drugs,and initial regimen

CO-RECEPTOR TROPISM ASSAYS

- Important when treatment with CCR5 antagonist is planned

- Usually done using a phenotypic assay

Even though HIV causes immune suppression, it causes hypergammaglobulinemia rather than hypogammaglobulinemia.

- Increased p24 antibody; basis for detection in window period
- T cell energy is commonly seen in HIV
- Abnormal response of T cells to mitogens is a test used in HIV.

DISEASE PROGRESSION[11]

After acute infection, HIV starts to destroy HIV-directed CD4+ cells; this process destructs the critical interaction between host CD4+ cells and CD8+ T cells and loosen the host CTL response. HIV highly seeds lymphoid organs and the central nervous system, the infection persists, and continued rounds of replication lead to the gradual depletion of CD4+ cell. Then activated, HIV-infected CD4+ cells returns to a dormant state remains latently infected. The CD4+ T cell count provides an correct way to assess the current immunologic status. HIV RNA level is strong predictor of the progression to AIDS in untreated HIV-infected persons.

CLINICAL MANIFESTATIONS

Acute HIV syndrome[12,13,14]

- Occurs in 50 – 70%
- Typical viral illness : fever, malaise, myalgia, arthralgias, LAP, etc.,
- It Occurs 3 – 6 wks after HIV infection

- Completely resolved in 2 – 4 wks
- High plasma viremia
- High levels of p24 antigenemia
    - HIVRNA by PCR is used for diagnosis in this stage
    - Seroconversion, i.e., antibody positive by 3 – 7 weeks after infection
    - Dendritic lineage cells are first to be infected
    - Dissemination of virus occur o lymphoid organs where infection persists.
    - CD8+ cytotoxic T lymphocytes are responsible for containment of primary infection.
    - Initially, low CD4+ and low CD8+ counts; later in acute stage (and also in advanced HIV); low CD4+ and high CD8+ - inversion of CD4/CD8 ratio.
- HIV escapes elimination from the body because of:
    - Deletion of CD8+ T cells due to overwhelming viremia
    - Sequestration of virus in lymphoid organs (cf CD8+ in peripheral blood) – NOT BECAUSE OF “MUTATION”.

- Possible neurological complications : meningitis, encephalitis, peripheral neuropathy, myelopathy

CLINICALLY LATENT PHASE

- Median time for untreated patients is 7 – 10 years
- Telescoped to 3 yrs in rapid progressors
- CD4+ counts decreases at the rate of 50 / mm3 per year
- Virus replicates in LNs (whether or not LAP+)
- One replication cycle = 1.5 days
- 10^{10} to 10^{11} virions produced per day
- 11/2 of infected CD4+ T cells is one day
- 11/2 of circulating virion is 30 minutes

When CD4 count is in normal range (500 – 1600 cells/cmm or 28 – 50%), the immune system defends itself against most antigens.

SYMPTOMATIC DISEASE[14]

200 – 500 CD4+ count

- Pneumococcal pneumonia
- Pulmonary tuberculosis
- Kaposi's sarcoma
- Herpes zoster

- Oral thrush
- Cryptosporidum
- Oral hairy leukoplakia

<200 CD4+ count

- Pneumocystis carinii pneumonia
- Candida esophagitis
- Recurrent/disseminated viral herpes simplex
- Toxoplasmosis
- Histoplasmosis
- Coccidioidomycosis
- PMLE
- Extra pulmonary tuberculosis

<50 CCD4 count

- CMV
- MAC
- Primary CNS lymphoma

RESPIRATORY SYSTEM[15]

- The most common manifestation is pneumonia
- The most common Opportunistic infection in HIV patients is Tuberculosis

- MC cause of pneumonia in HIV patient: Pneumococcal

Pneumocystis jiroveci[16,17]

- Usually occurs in patients with CD4+ <200
- Transmission is airborne
- Pathology : binds to and damages type I pneumocytes; remains extracellular….and there is hypertrophy of type II pneumocytes.
- Presents with fever, nonproductive cough, retrosternal burning, pleuritic pain, dyspnea
- Tachypnea, tachycardia, cyanosis
- Chest exam : no findings / bibasilar rales
- CXR : Normal in early disease and bilateral faint interstitial infiltrate later. And there is no lymph node enlargement and pleural effusion.
- 'Classic' finding of dense perihilar infiltrate is unusual
- Patients on AEROSOLIZED PENTAMIDINE for prophylaxis can manifest with Upper lobe cavities, pneumothorax, extrapulmonary commonly lymphnode.
- Hypoxemia, ↑LDH

DIAGNOSIS

Demonstration of trophozolte / cyst is must

- ***Silver Methenamine stain, Wright Geimsa-stain***

  Sputum induction

  Brancho-alveolar lavage

  Trans-bronchial lung biopsy

- Treatment of choice: TMP / SMZ (dose: 15-20/75-100 mg/kg/d) for 21 days.
- S/E: rash, BM suppression, hepatitis, hyperkalemia quite common in HIV patients.
- If pO2 <70mmHg OR (A-a) O2>35mmHg: ADD CORTICO STEROID.
- Treatment in patient sensitive to sulfonamides: Pentamidine
- Prophylaxis: 1 DS tablet of Cotrimoxazole daily.

INDICATIONS

All patients with prior PCP

CD4+ count less than 200/cumm

Pyrexia of unknown orgin

Oro-pharyngeal candidiasis

(This also provides prophylaxis against Toxoplasmosis, nocardiosis and bacterial infection.

Alternative drugs for prophylaxis: Pentamidine/ Dapsone/ Pyrimethamine/ Atovaquone

TUBERCULOSIS

The number of HIV positives in India around 3.97 million cases. In AIDS affected cases, sixty percentage of patients had TB.

HIV AND TB

Early Disease (High CD4 count)

Pulmonary disease more common

Upper lobe

Cavitation +

Mediastinal Lymph Nodes -

Sputum positivity rate-higher

Constitutional symptom – common (incl. cough and hemoptysis)

Late Disease(Low CD4 count)

Extrapulmonary disease commoner than pulmonary

Lower lobe

Cavitation

Mediastinal lympadenopathy

Sputum usually negative

Uncommon

Treatment of Tuberculosis in HIV affected patients

- Anti-Tuberculosis treatment is the same for both HIV infected and negative TB patients, except of the using the thiocetazone. Thiacetazone having severe cutaneous reactions like Exfoliative Dermatitis , Steven Johnson syndrome and it can be fatal.

- In place of TZN, use EMB in HIV+ve persons.

- NRTIs can be safely co-administered with ATT.

WHO recommendations

- It recommends that people with TB/HIV complete their Tuberculosis treatment prior to start ART unless there is a high chance of HIV disease progression and death during the period of tuberculosis treatment (i.e. a CD4 count <200/mm3 or disseminated TB).

- Where a person needs Tuberculosis therapy and ART concurrently, first line treatment include ZDV/3TC (lamivudine) or d4Tn (Stavudine)/3TC plus either an NNRTI or ABC (Abacavir).

- If patient need NNRTI-based therapy, EFZ (Efavirenz) would be the preferred drug as it aggravates the hepatotoxicity of TB treatment appears less compared to Nevirapine.

- HIV affected patients are not recommended during Tuberculosis therapy with rifampicin, except ritonavir.

MAC

- Mycobacterium avium intercellulare complex usually occurs in patients with CD4+ <50

- M. avium commoner than M. intracellulare

- Prior infection with M. tuberculosis decreases risk of MAC

- Most commonly presents with fever, weight loss, night sweats: sometimes abdominal pain, diarrhea, LAP

- Chest x ray shows bilateral lower lobe miliary shadows

  Diagnosis : culture of blood / involved tissue e.g. sputum

- Treatment : Clarithromycin + Ethambutol + Rifabutin (or rifampicin) / amikacin / ciprofloxacin

- This treatment is continued till the time patient achieves CD4+ count more than 100/mm3 for more than 6 months.

- Primary Prophylaxis is given to patients with CD4+ count <50/mm3 in the form of Tablet Azithromycin 1200 mg once a week.

- Rhodococcus, Cryptococcus, coccidiodomycosis can cause lung parenchymal disease with cavitation.

NEUROLOGIC SYSTEM[18]

Opportunistic cns infections:

- Toxoplasmosis
- Cryptococosis
- CMV
- HTLV-1
- PML by JC virus
- Amebiasis

NEOPLASMS

- Primary CNS Lymphoma.
- Kaposi s sarcoma

MYELOPATHY

- Vacuolar myelopathy
- Pure sensory ataxia

PERIPHERAL NEUROPATHY

- Acute and chronic inflammatory demyelinating poly neuropathy.
- Mononeuritis multiplex.
- Distal symmetric poly neuropathy.

ASEPTIC MENINGITIS AND MYOPATHY

AIDS DEMENTIA COMPLEX[19]

- Also known as HIV encephalopathy.
- Occurs in late stage of hiv infection and sub-cortical dementia..
- Manifestations are Lack of concentration, forgetfulness, difficulty performing complex tasks, ataxia, tremor.
- In contrast to Alzheimer's disease (cortical dementia) aphasia, apraxia, agnosia are rare.
- Bladder bowel involvement occurs in late stages.
- The level of Alertness is normal. (no detrioration in level of consciousness).

- Severity of cognitive dysfunction increases with declining immune function. And low CD4 count.
- Most common cause of seizures in HIV, 24 to 47% of first seizure due t HIV encephalopathy.
- Improvement in cognitive function occurs with ART.

Causes of seizure in HIV patient[19]

- Toxoplasmosis
- Tuberculosis
- PML
- Cryptococcal meningitis
- Metabolic and electrolyte disturbances
- Drugs

ORAL

Infections

Fungal

- Candidiasis
- Systemic fungal infection with oral lesion
- Histoplasmosis
- Cryptococcosis
- Aspergillosis

Viral

- Oral hairy leukoplakia EB virus
- Herpes simplex CMV
- Varicella zoster
- Papilloma virus

Bacterial

- Periodontal infection

Neoplasm

Carcinoma

- Squamosus cell Ca
- Basal Cell Ca
- Sarcoma
- Kaposi sarcoma

Lymphoma

- NHL
- Idiopathic oral aphthous ulcers
- HIV salivary gland disease.

Gastrointestinal manifestations[20]

- Esophageal disease
  - Esophagitis – Candida, CMV, HSV
- Gastric disease

- Gastric lymphoma
- Atypical presentation of secondary infections
- Leutic gastritis
- Gastric TB

➢ Intestinal manifestations

- Diarrhoea

BACTERIAL INFECTION

Salmonella

Shigella

Campylobacter

Clostritium difficle

PARASITIC INFECTIONS

Small intestine

Cryptosporidium

Isospora

Microsporidia

Giardia

LARGE INTESTINE

Entamoeba histolytica

Mycobacterial

- MAC
- M.Tuberculosis

Viral

- CMV – Colitis
- Herpes simplex

RECTAL LESIONS

Infections

Perirectal ulcers

HSV

Condylomata acuminata

Neoplasm

KS

IMPORTANT GIT MANIFESTATIONS

Esophagitis [20]

- Candida – is the most common infection and AIDS defining illness and oral candidiasis is associated with dysphagia , odynophagia.
- Definite diagnosis is possible on endoscopic biopsy.
- CMV- single large ulcer
- HSV- multiple small ulcer

Diarrhea

- The most common protozoan causing diarrhea : Cryptosporidium
- Other causes are microsporidia, isospora belli, c.jejuni, shigella, salmonella.

HIV ENTEROPATHY / AID ENTEROPATHY

- Diarrhea for >1 month
- No identifiable cause of diarrhea despite extensive evaluation even after upper and lower GI endoscopy..
- Low grade Mucosal atrophy indicates hyporegenerative state and diminished or absent small intestinal lactase leads to lactase deficiency causes malabsorption and weight loss.

HEPATOBILIARY DISEASES[20]

- High incidence of HBV & HCV in HIV because of similar routes of transmission.
- 95% of HIV infected patients have evidence of prior/active HBV infection, of which 10% are HBsAg+ve 5 – 40% have HCV co-infection.

HBV CO-INFECTIONS[21]

- Increased in chronic HBV infection (HBsAg positivity after acute infection)
- Decreased in inflammatory liver disease (lower ALT, milder histology)
- BUT higher viral replication of HBV. There is 10 folds increased mortality in patients with active infection.
- Lamivudine , emtricitabine, adefovir, tenofovir and entecavir , telbivudine alone or in combination are useful in treatment of hepatitis B in patients with HIV infection.

HCV CO-INFECTION

- More severe hepatitis and worse prognosis than with HCV alone
- Increased incidence of liver failure
- Lack of sensitivity of serological tests (anti-HCV) in diagnosing HCV infection.
- perinatal and heterosexual transmission.
- Treatment is pegylated interferon α with ribavirin

CO-INFECTION OF HEPATITIS B OR C

- The possibility of additive hepatotoxicity regimens with dd1/d4T and/or NVP would be avoided in patients having active hepatitis.

- 3TC and TDF are highly active against hep B and new infection

TREATMENT HIV INFECTION INCLUDES

- Anti retroviral therapy and management of opportunistic infections.

- Prophylactic interventions

Table – Indications for the initiation of ART [22,23,24]
Acute infection syndrome
Chronic infection a. Symptomatic state (including HIV-associated nephropathy) b. Asymptomatic state 1. CD4+ count <500/L 2. Pregnancy
Postexposure prophylaxis

Antiretroviral therapy

Combination ART therapy or highly active antiretroviral therapy (HAART) is the major role in management of patients with HIV infection.

TO CHANGE THE REGIMEN-THE FOLLOWING PRINCIPLES ARE UESD

- Single drug would not be added or changed to a falling regimen; only if resistance testing has been done and it shows resistance to one drug, then to change one drug only.

- Cross-resistance among NNRTIs is common and therefore changing between NNRTIs should be avoided in PI therapy; nelfinavir should always be given first.

- Cross resistance in common between ritonavir and indinavir and changing between these 2 drugs should be avoided.

Immune Reconstitution Syndrome

- TB is the common opportunistic infection.

- For patients with TB, this syndrome occurs in about 30% of patients.

- The syndrome is manifested by fever, lymphadenopathy, pulmonary lesions (by X-ray) and expanding central nervous systems lesions.

- Typically self-limited one, to start the use of a short course of corticosteroids.

- ART would not be stopped for immune reconstitution syndromes and antimicrobial therapy for the OI should be started with ART.

Post Exposure Prophylaxis (PEP)

- The rationale in PEP is that systemic infection does not occur immediately after an exposure, leaving a brief window of opportunity during which post exposure antiretroviral intervention may modify or prevent viral replication.

- PEP should be initiated preferably within 1 to 2 hours post exposure and up to 36 hours. PEP should be discouraged 72 hours after exposure. It should be administered for 28 days.

ARV REGIMEN

Basic Regimen : Zidovudine 300 mg BD + Lamivudine 150 mg BD for 28 days (Or) Stavudine 30/40 mg BD + Lamivudine 150 mg BD

Expanded Regimen : Above regime + Indinavir 800 mg tds for 28 days (Or) Above regimen + Efavirenz 600 mg HS for 28 days.

The health care worker should be tested for HIV as per the following schedule:

- Baseline HIV: At the time of exposure
- Repeat HIV: At 6 th week, 12 th week and 6 month following exposure.
- Pre and post test counseling should be needed.

During this period, HCW should not:

Donate blood / semen / organs

Indulge in unprotected sex

Breast feed her infant

Become pregnant

New Drugs

Ritonavir

Indinavir

Nelfinavir

Atazanavir

Tipranavir

Darunavir

Maraviroc

Entry inhibitors

Enfuvirtide

Changing the ART regimen if

- Less than a one-log drop in plasma HIV RNA by four weeks following ART.
- A reproducible significant increase from the nadir of plasma HIV RNA level not attributable to intercurrent infection, vaccination or test methodology.
- Persistently declining CD4+ T cell numbers
- The adverse effects of the ART.
- Patients clinical detoriation.

NEW DRUGS : RECENT ADVANCES

Entry Inhibitors:

Maroviroc

Enfuvirtide

Acts by inhibiting virus entry via CCR5 coreceptors

It doesn't inhibit virus taking entry with the help of CXCR4

Very potent drug and resistance is difficult to develop

Side effectS.

Hepatotoxicity

Hypotension due to alpha blockade.

Rash

Hypersensitivity

VIRAL INTEGRASE INHIBITOR

Raltegravir

Elvitegravir

- Used in resistant HIV infection
- Used in combination as a part of HAART
- Does not cause lipodystropy.

HIV ENDOCRINOPATHY

The every endocrine organ can affected by HIV, may leads to functional derangement of that endocrine gland. A pandemicity of HIV and survival benefit of HAART makes high incidence of endocrinopathies in last two decades.

HIV Endocrinopathy - currently a new emerging field of modern Medicine.

HIV Endocrinopathy grouped into [25-27]

- Primary
- Secondary .

Primary

Related to direct effect of human immunodeficiency virus itself.

Secondary

Related to indirect effect of HIV mediated by

1) Cytokine
2) Immune reconstitution.
3) Opportunistic infections
4) HAART
5) Rarely neoplasms.

The Endocrine abnormalities seen in early and late stages of HIV infection.

The Commonly involved endocrine organs are

1) Adrenal Gland
2) Gonads
3) Thyroid gland
4) Pituitary and hypothalamus
5) pancreas

The involvement of endocrine organ leads in poor quality of life and significant mortality and morbidity.

- There is more complex interaction between HIV and Endocrine organs which can leads to variable [mild to severe] changes in hormone secretion , transport , metabolism. Rarely hormone resistance and organ failure seen in HIV patients.

PATHOPHYSIOLOGY OF HIV ENDOCRINOPATHY

1.The progressive immune dysfunction caused by HIV alters the internal environment by activation of cytokines, chemokines, antibody formation, and by immune reconstitution .

The relation between HIV and Endocrine function , secretion mainly centers on immune modulatory effect of cytokines at every level of endocrinal axis [Hypothalamo – Pitutary –Effector organ]

The adrenal gland a main target organ in HIV and adrenalitis is well known entity..[28-30]

HIV Infection triggers the activation of macrophage to secretes interleukins -1 , and tumor necrosis factor a potent adrenal stimulator.[31-32]

HIV infection may cause polyclonal B cell activation and production of antibodies against glandular cells , there by inhibiting glandular endocrine function.[33]

2. Structural Destruction Of Endocrine Tissue:

In HIV every endocrine organ can secondarily affected by

- Opportunistic infections
- Hamorrhage
- Neoplastic process
- Other nonspecific inflammation.

- Adrenal destruction mostly caused by CMV in 40 to 90% of HIV Adrenalitis.[34] Other causes are - mycobacterium tuberculosis, MAC, Cryptococcus, and hemorrhage.

- Pnemocysti thyroiditis cause painful thyroiditis may leads to hyper followed by hypothyroidism.[35]

- Pitutary and Hypothalamus destruction can also caused by Toxoplasmosis, Cryptococosis , CMV infection.

3. Endocrine Effects of Medications

Medications used in HIV can cause endocrine dysfunction commonly, they primarily contributes to the alterations in

1) Lipid Metabolism

2) Insulin Sensitivity

3) Bone mineral Homeostasis.

4) Fat Redistribution.

5) Lipid Profile.

PROTEASE INHIBITORS [36-37]

May have direct effects on Adipogenesis via

- Decreased nuclear localization regulatory element binding protein [SREBP-1].
- Reduction in peroxisome proliferator activated receptor gamma [PPAR gamma].
- Other relevant endocrine effects are Fat Redistribution, Hypertriglyceridemia, and increased production of small dense atherogenic LDL 2 molecules.
- PIs can cause decreasing GLUT4 activity and Insulin Sensitivity resulting in Hyperglycemia.

NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS [38]

- Like PIs, NRTI also causes fat redistribution, hyperglycemia, loss of appetite, Subcutaneous fat loss, gynecomastia.
- Can also cause Renal tubular dysfunction..

NUCLEOTIDE REVERSE TRANSCRIPTASE INHIBITORS

- Tenofovir Metabolised by plasma esterase, associated with fat redistribution and hypophophatemia.

NON- NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS [39-40]

These drugs metabolized by cytochrome pathways, and are associated with hyper lipidemia , fat redistribution..

Drugs other than anti retro viral , in addition antifungal , antibiotics, chemotherapeutic agents used in opportunistic infections in HIV patients can also have adverse effect on Endocrine function.

Idiopathic adrenohypophyseal necrosis [41] observed in 10% of HIV patients thought to be direct effect of hiv.

Hyper prolactinemia and gynecomastia reported in more than 20% of HIV patients and associated with increased CD4 count, thought to be HIV infection reduces the dopaminergic tone and increases the bioactivity of prolactin[42,43]

HYPOGONADISM[44-46]

Primary

HIV induced immunomodulators causes

TNF Mediated inhibition of steroidogenesis by altering the side chain cleavage.

IL-1 Prevents leydig cell steroid production and leutinizing hormone binding to leydig cells.

Secondary

- Hypogonadism in HIV patients mostly secondary .
- Low Gonadotropin Level due to the effects of ,[47]
  - Under nutrition.
  - Infection - Inflammation.
  - Drugs effects on gonadotropin production..
- Clinically, male patients with advanced disease have,

  Loss of libido – 67%

  Impotence – 33%
- Ovarian Dysfunction in female is less common, can cause Amenorrhoea around 25% patients during stress of illness, Anovulation seen in half of patients with low CD4 count[48,49]
- Early Menopause up to 8% of HIV infected female patients.

PANCREATIC DYSFUNCTION[50,51]

- A target organ of opportunistic infection, and malignancies [lymphoma, Kaposi sarcoma].
- Pancreatitis and hypoglycemia are major clinical manifestations..
- Pancreatitis commonly caused by drugs Didanosine , Zalcitabine, Trimethoprim, Pentamidine[52-54] .
- Hypoglcemia results from islet cell inflammation and insulin release.

HIV AND THYROID DYSFUNCTION:

Thyroid Gland: [55]

In Greek Thyreos means - Shield, Eidos means - Form.. Thyroid Gland located in anterior to trachea, and consists of two lobes, connected by isthmus..

- The Normal Size of Thyroid gland is 12 to 20 gram.
- Throid Gland Develops from the floor of primitive pharynx during 3 rd week of Gestation and its Migrates along Thyroglossal duct to reach Neck..

Thyroid Hormone Synthesis begins at 11 week of gestation.

- Thyroid Gland produces thyroxine [T4], and Tri iodothyroxine [T3] , and these Hormones acts through recptor alpha and beta.. Regulation of thyroid gland function via HYPOTHALAMO – PITUTARY-THYROID AXIS.

- TSH and TRH Secreted from hypothalamus and pitutary gland respectively, control over thyroid gland function in a feedback manner.

- Thyroid hormones plays critical role in CELL DIFFERENTIATION during development , and maintain Metabolic , Thermogenic HOMEOSTASIS.

THYROID FUNCTION ABNORMALITIES

- Hypo thyroidism : low free T3 , T4 and increased TSH.

- Subclinical hypothyroidism : Normal Free T3, T4, and increased TSH.

- Hyperthyroidism : Increased Free T3 , T4 and undetectable or low level TSH.

- Subclinical hyper thyroidism : Normal Free T3, T4, and Low level of TSH.

- Central hypothyroidism : Both TSH and Free T3, T4 are decreased.

CLINICAL FEATURES OF THYROID DYSFUNCTION:

Hypothyroidism

Symptoms

- Constipation
- Weight gain
- Hoarseness of voice
- Cold intolerance
- Dry skin

Signs

- Bradycardia
- Delayed tendon reflex
- Carpal tunnel syndrome.
- Serous cavity effusion.

CLINICAL FEATURES OF HYPERTHYROIDISM:

Symptoms

- Palpitation.
- weight loss.
- Diarrhoea

- Irritability.
- Heat intolerance.

Signs

- Tremors.
- Lid lag.
- Tachycardia, arrhythmias.
- Proximal myopathy.
- Gynecomastia.

LABORATORY TESTS FOR THYROID FUNTION

- Measures TSH and Free or Unbound T3, T4 levels.
- Antibodies to thyro peroxidase and thyroglobulin..
- Radioactive iodine uptake.
- Ultrasonogram neck.

THYROID DYSFUNCTION IN HIV [55]

- Thyroid function alters in 10 to 15% of HIV patients.
- Most asymptomatic HIV patients with stable body weight maintain normal thyroid gland function..[56-57]
- Among HIV patients 1 – 2% have overt hypothyroidism and about 35% patients may have subtle abnormality. [58- 60]

The abnormalities of thyroid gland function in HIV patients may be due to [61-62]

- Direct effect of HIV itself.
- Opportunistic infections infiltrates or infect thyroid gland.[63-65]
  - Cryptococcus neoformans.
  - Cytomegalo virus.
  - Visceral leishmaniasis.
  - Suppurative bacterial infection.
  - Mycobacterium tuberculosis.
  - MAC
  - Histoplasmosis
- Neoplastic infiltration
  - Kaposi sarcoma.
  - Lymphoma.
  - Occult papillary carcinoma.
- Effects of Highly active antiretroviral therapy.
- Stress Of Advanced Disease.

The Various Thyroid function abnormalities seen in HIV patients these are,

- Subclinical Hypothyroidism.
- Overt Hypothyroidism.
- Immune Reconstitution Graves Disease.
- Isolated Low T4 Level.
- Non thyroidal Illness or Sick Euthyroid Syndrome.

Beltran et al studied thyroid function abnormalities in 350 HIV patients and reported that , increased prevalence of primary hypothyroidism in HIV patients.[66-67]

Studies showed,

Overt hypothyroidism - 2.6%

Subclinical hypothyroidism - 6.6%

Isolated FT4 Level - 6.8%

Among 350 HIV patients studied

Beltran et al and Quirine et al , collazos et al[68] reported the prevalence of sub clinical Hypothyroidism in both ART naïve as well as in patients on ART were similar..

In Contrast, Nelson et al [69] and calza et al [70] reported as high prevalence of subclinical hypothyroidism in patients on HAART..

Hepatitis co infection associated with Hypothyroidism mediated by autoimmune process or by adverse effects of IFN alpha therapy..[71-72]

RISK FACTORS FOR THYROID DYSFUNCTION IN HIV[73-75]

- ❖ Low CD4 count.
- ❖ Male sex.
- ❖ Longer Duration HIV infection.
- ❖ Older Age.
- ❖ Co Infection with Hepatitis C virus.
- ❖ Patients on HAART.
- ❖ Opportunistic infections.
- ❖ Immune Reconstitution.

INDICATION FOR THYROID TESTING IN HIV PATIENTS[76]

- Symptoms of Hypo or Hyperthyroidism.
- Osteopenia.
- Dyslipidemia
- Depression.
- Arrythmias [Atrial fibrillation].

ISOLATED LOW T4 LEVEL[77-81]

- Especially patient on HAART.
- Reported prevalence 1.3 to 6.8 %.
- In HAART didanosine , stavudine and ritonavir associated with this condition[82]

SUBCLINICAL HYPOTHYROIDISM

The most common thyroid abnormality in HIV patients on HAART, with elevated TSH Level and normal T3, T4..

The Prevalence of Subclinical Hypothyroidism in,[83]

General population - 4.3%.

HIV patients on HAART - 3.5 to 12.2%.

Anti thyro peroxidase antibodies seen in,

- 50 to 80% of SCH patients in general population.[84-85]
- Among SCH in HIV Patients , the anti TPO abs rarely identified. And suggest the etiology may not be autoimmune itself.

Beltran reported subclinical hypothyroidism in HIV patients associated with Low CD4 count and stavudine therapy. [86]

OVERT HYPOTHYROIDISM

The Prevalence overt hypothyroidism in various studies in HIV patients are,

Beltran et al - 2.6%

Madge et al - 2.5%

Nelsons reported ,

The expected incidence of hypothyroidism in patients on HAART, and recommends Universal Screening of HIV patients on therapy.

The prevalence of hypothyroidism:[87,90]

- In general population - 0.3%
- In HIV infected patients varies - 0 to 2.6%.

May be associated with anti TPO antibodies.

GRAVES DISEASE

- Commenest among HIV immune reconstitution syndrome,

Prevalence[91]

Woman - 3%.

Men - 0.2%.

- Autoimmune mediated production of anti TSH receptor antibodies.

- It is the leading cause of overt hyperthyroidism in both general population and HIV patients.
- In HIV patients may occurs after immune restoration by HAART and it is most commonly diagnosed at 12 – 36 months after HARRT initiation.[92]
- IFN alpha used in hepatitis C infection also associated with graves disease.
- Radioactive iodine uptake study shows high uptake in graves disease and Low uptake in thyroiditis..

MANAGEMENT OF THYROID DYSFUNTIONS IN HIV PATIENTS:

Overt Hypothyroidism.[93]

- Treated with levothyroxine and maintain TSH Level at 0.5- 2.5 Mu\L.
- Drug interaction between protease inhibitor and levothyroxine also reported due to shared glucuonidation pathway

Subclinical Hypothyroidism.[94,95]

- In HIV Patients with sub clinical hypothyroidism , recheck TSH Level 1 – 2 months Later.

- In general population TSH Normalize within 1 year in about 30% of patients,, but in HIV patients the proportion of normalization level may be Lower.
- If TSH Level persists more than 10 Mu\L may considered treatment with levothyroxine.
- Patients may treated with thyroxine if symptoms of hypothyroidism or pregnancy, dyslipidemia, with TSH level between 5.5 to 10 Mu/L..

Hyperthyroidism.[96]

- Treatment Depends on underlying cause.
- In case of Graves disease treated with antithyroid drugs , and definitive treatment with radioiodine ablation, or surgery may be appropriate in some patients.
- Toxic multi nodular treated with radioiodine ablation or surgery.
- Sub acute thyroiditis treated with NSAIDS or STEROIDS.
- Regardless of cause patients with hyperthyroidism treated with beta blocker for control over hyper adrenergic symptoms.

- Various studies shows that TSH negatively correlate with CD4 count and positively with HAART.

Various studies shows that there is negative correlation between TSH and CD4 count…positive correlation with free T3 and free T4 and HAART therapy.

Abnormal thyroid function common among in HIV patients especially during HAART.

Currently insufficient evidence in favor of screening for thyroid abnormalities in asymptomatic HIV patients ,, and need further Larger studies.[97]

Thyroid involvement in HIV infection confirmed by various studies and exact mechanism still unknown., may be related to direct effect of virus, opportunistic infection, autoimmune , medication to treat HIV.

Thyroid hormone plays a fundamental role in metabolism and immune both cellular and humoral regulation, and recognition of these abnormalities may contributes to complete the characterization of different stages the HIV infection and their treatment and may be important for a better management of hiv patients..

Larger studies are needed to examine the epidemiology and health consequence of mild thyroid function abnormlities in HIV patients and to better screening and treatment guidelines.

MATERIALS AND METHODS

This case control study was conducted in the Rajiv Gandhi Government General Hospital , Madras Medical College in the department of institute of internal medicine in 2014.

The total number of patients to be studied in the study was 100. Patients are selected from people attending OPD at ART CENTRE madras medical college and Ethical Committee clearance was obtained for this study..

STUDY CENTER

Rajiv Gandhi Government general hospital, Madras Medical College.

STUDY DURATION

6 Months – April 2014 to September 2014.

STUDY DESIGN

Cross Sectional Observational Study.

INCLUSION CRITERIA

1) Age more than 18 years

2) HIV patients irrespective of stage on HAART.

3) Sex - both male and female

4) Patient willing to give written informed consent.

EXCLUSION CRITERIA:

1) critically ill patients.

2) Known thyroid disease patients.

3) Aged less than 18 years.

CLINICAL PROFILE

The following parameters assessed in HIV patients on HAART.

1) Age and sex

2) Stage of HIV infection.

3) ART regimen

4) Duration of therapy

5) Symptoms of thyroid dysfunction.

SYMPTOMS

Regarding hypothyroidism - constipation, weight gain, cold intolerance, fatigability, menorrhagia, hoarseness of voice.

Regarding hyperthyroidism

Irritability, dysphoria, diarrhea, polyuria, oligomenorrhea, palpitations, heat intolerance.

PHYSICAL EXAMINATION

- Thyroid examination.
- Pulse rate and blood pressure.
- Dry skin
- Tremors
- Ocular examination.

LABORATORY PARAMETERS

Biochemical

- THYROID FUNCTION TEST .
- CD4 COUNT.

Thyroid functiontest.

TSH - using ultra sensitive sandwich chemi luminescent immuno assay.

FREE T4 and FREE T3 - using competitive chemi luminescent immuno assay.

Patients symptoms and thyroid function test , CD4 count analyzed with various parameters.

Overt hypothyroidism

- low free T3 and T4 with elevated TSH.
- Sub clinical hypothyroidism:
- Normal free T3, T4 and elevated TSH level.
- Overt hyperthyroidism:
- Elevated free T3 , T4 and very low or undetectable TSH.
- Sub clinical hyperthyroidism:
- Normal free T3, T4 and very low or undetectable TSH.

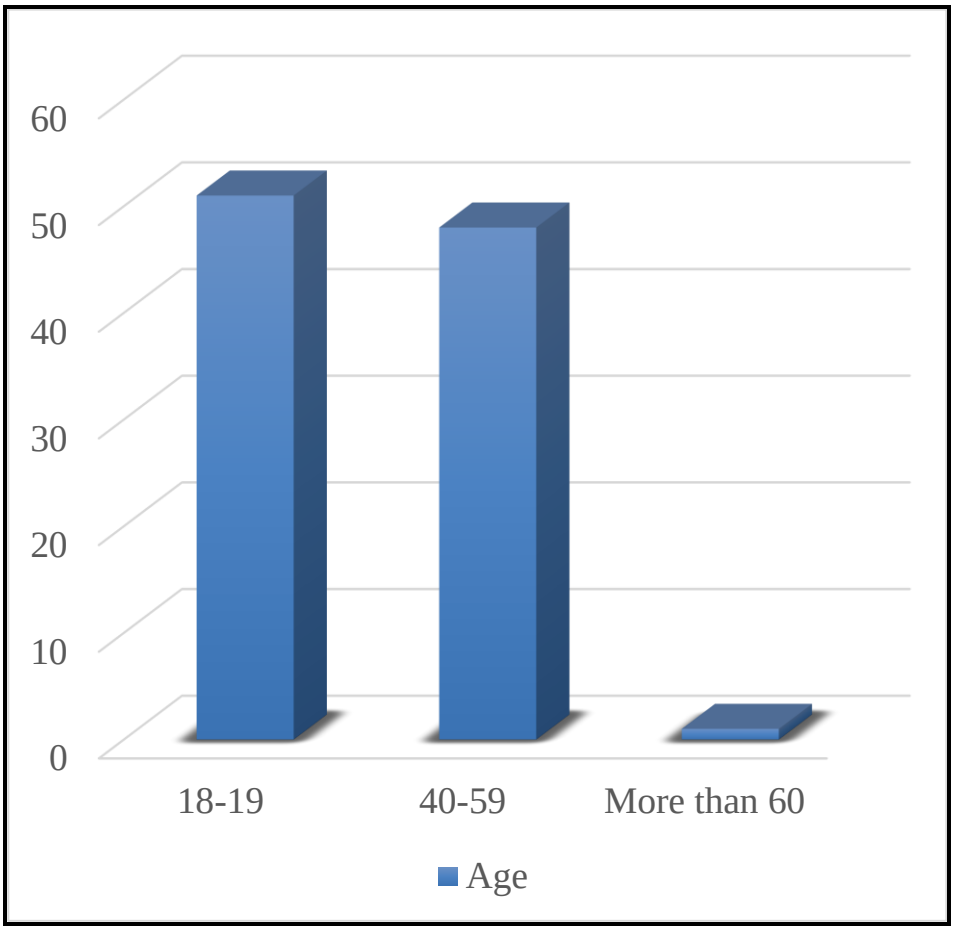
The symptoms and signs, biochemical parameters were done in each patient and analyzed with appropriate statistical method.

OBSERVATION AND RESULTS

FREQUENCY TABLE

Table A: Age distribution of studied patients:

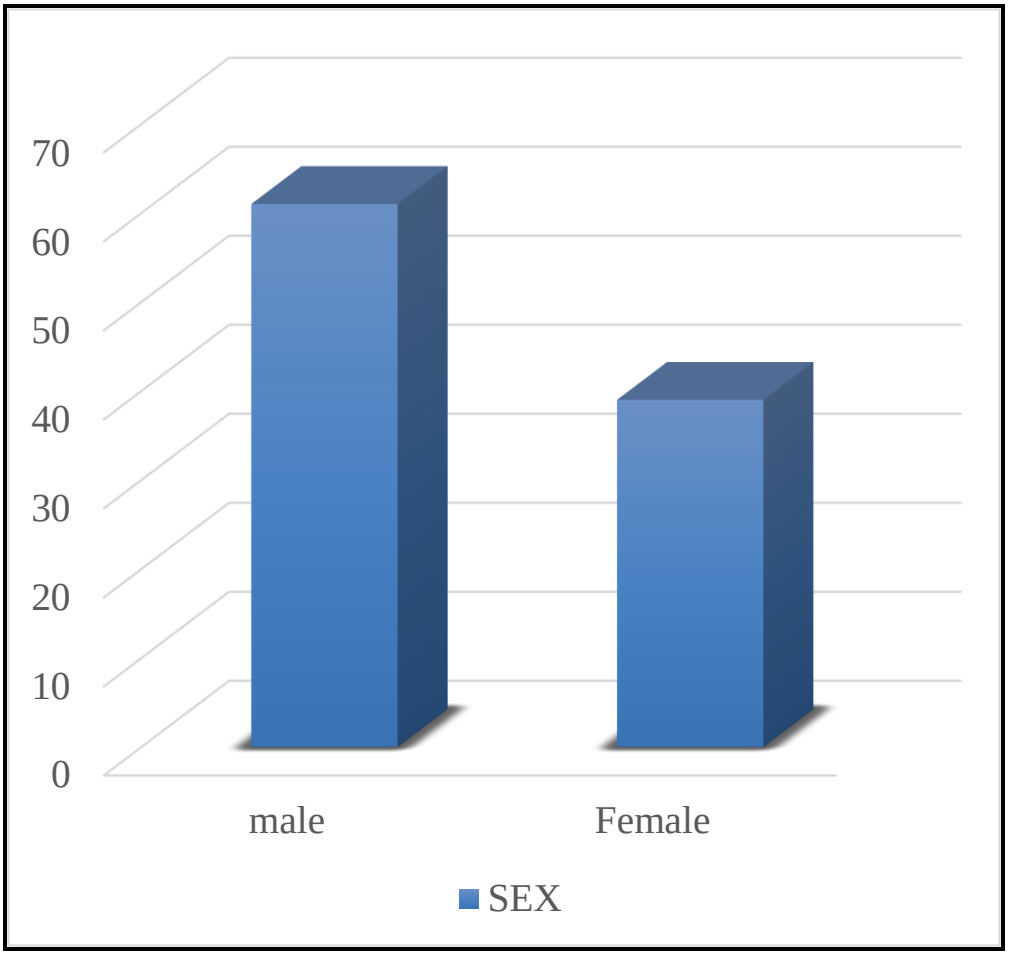
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	18-39	51	51.0	51.0	51.0
	40-59	48	48.0	48.0	99.0
	> 60	1	1.0	1.0	100.0
	Total	100	100.0	100.0	



Distribution of age among studied population.

Table B: Sex distribution of studied patients

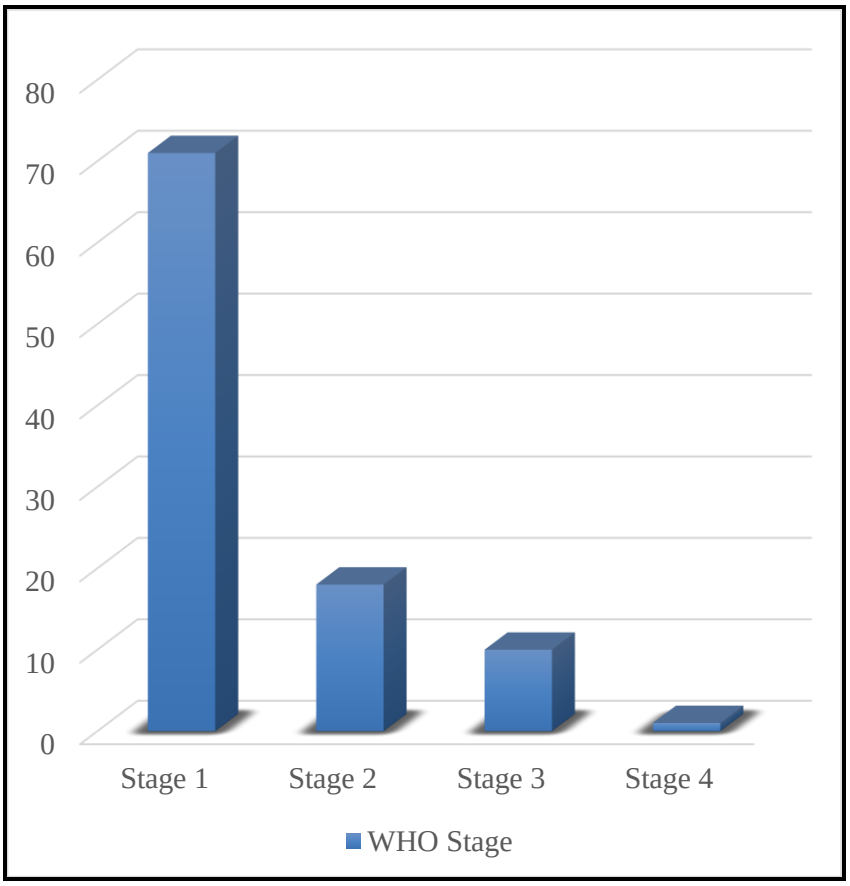
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Male	61	61.0	61.0	61.0
	Female	39	39.0	39.0	100.0
	Total	100	100.0	100.0	



Distribution of sex among 100 studied patients. Males were 61 and Females were 39 in our study group.

Table C: Disease stage distribution of studied patients

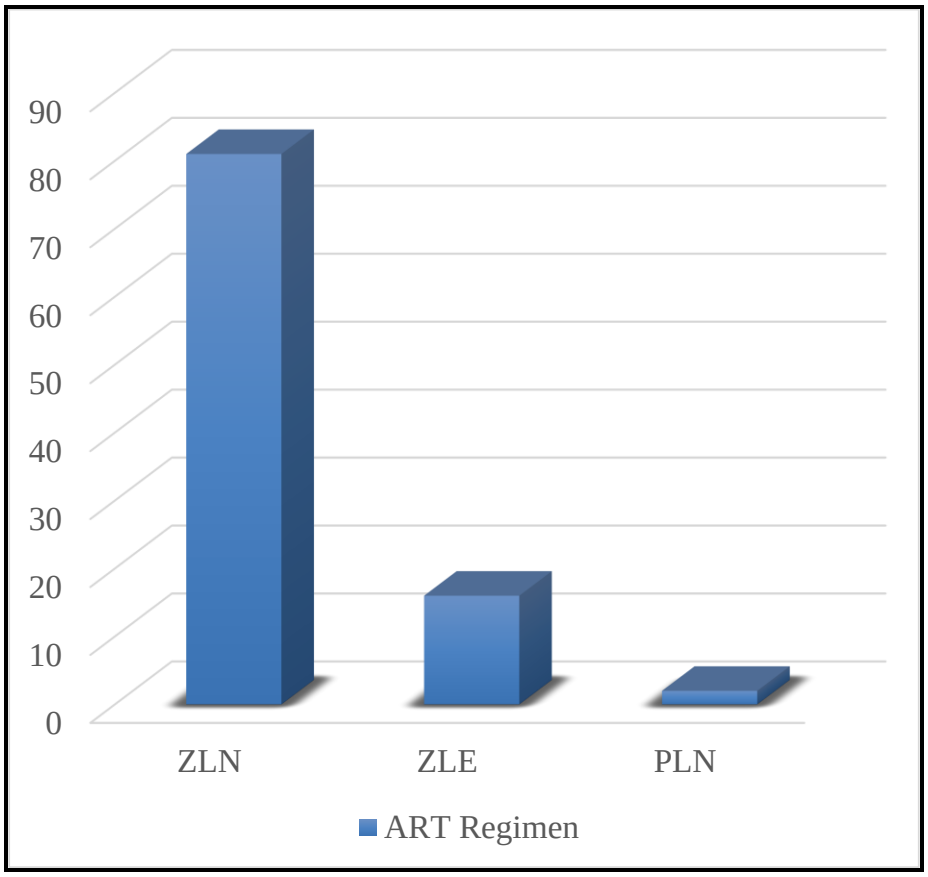
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	I	71	71.0	71.0	71.0
	II	18	18.0	18.0	89.0
	III	10	10.0	10.0	99.0
	IV	1	1.0	1.0	100.0
	Total	100	100.0	100.0	



Distribution of HIV stage among study populatioN. 71% Patients Are In Stage 1

Table D: ART regimen distribution of studied patients

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	ZLN	82	82.0	82.0	82.0
	ZLE	16	16.0	16.0	98.0
	TLN	2	2.0	2.0	100.0
	Total	100	100.0	100.0	

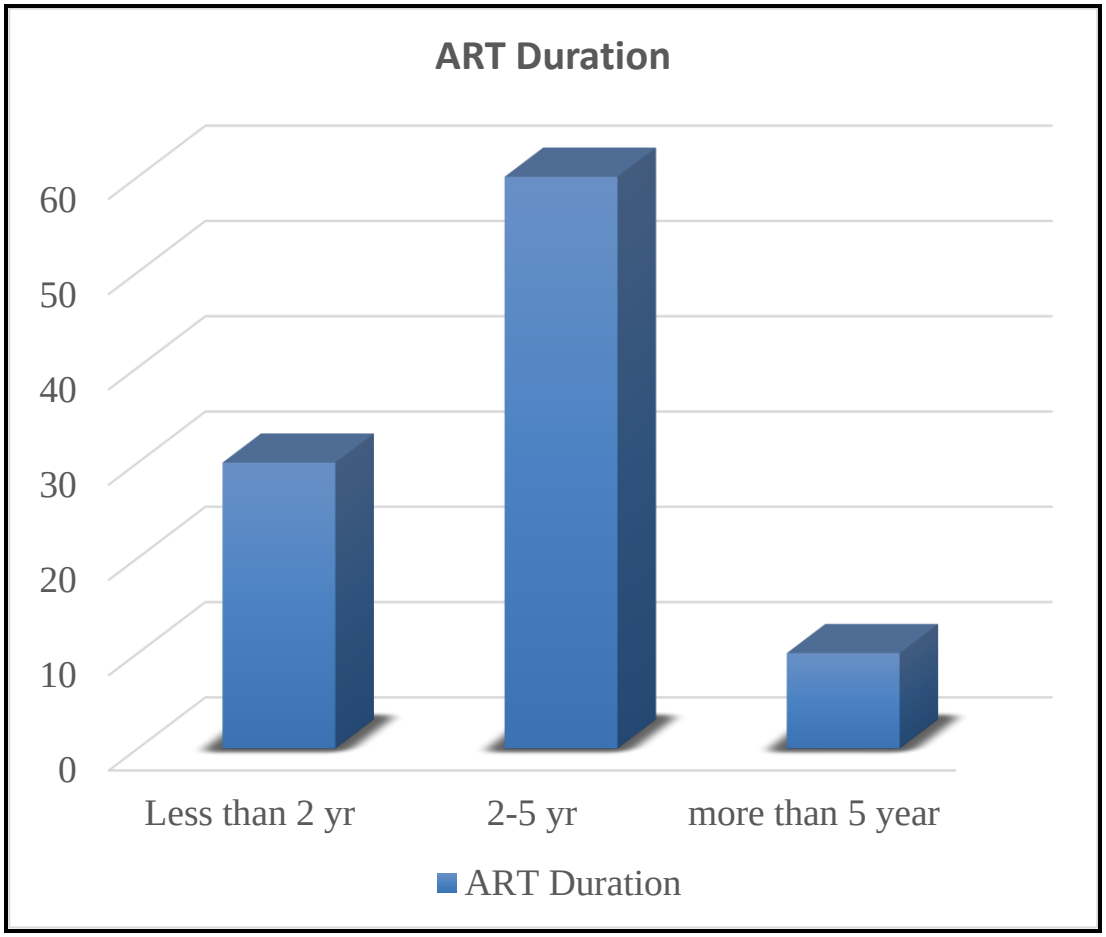


Distribution of ART regimen in study population.

Most of patients are in ZLN regimen- 81%

Table E: ART duration distribution of studied patients

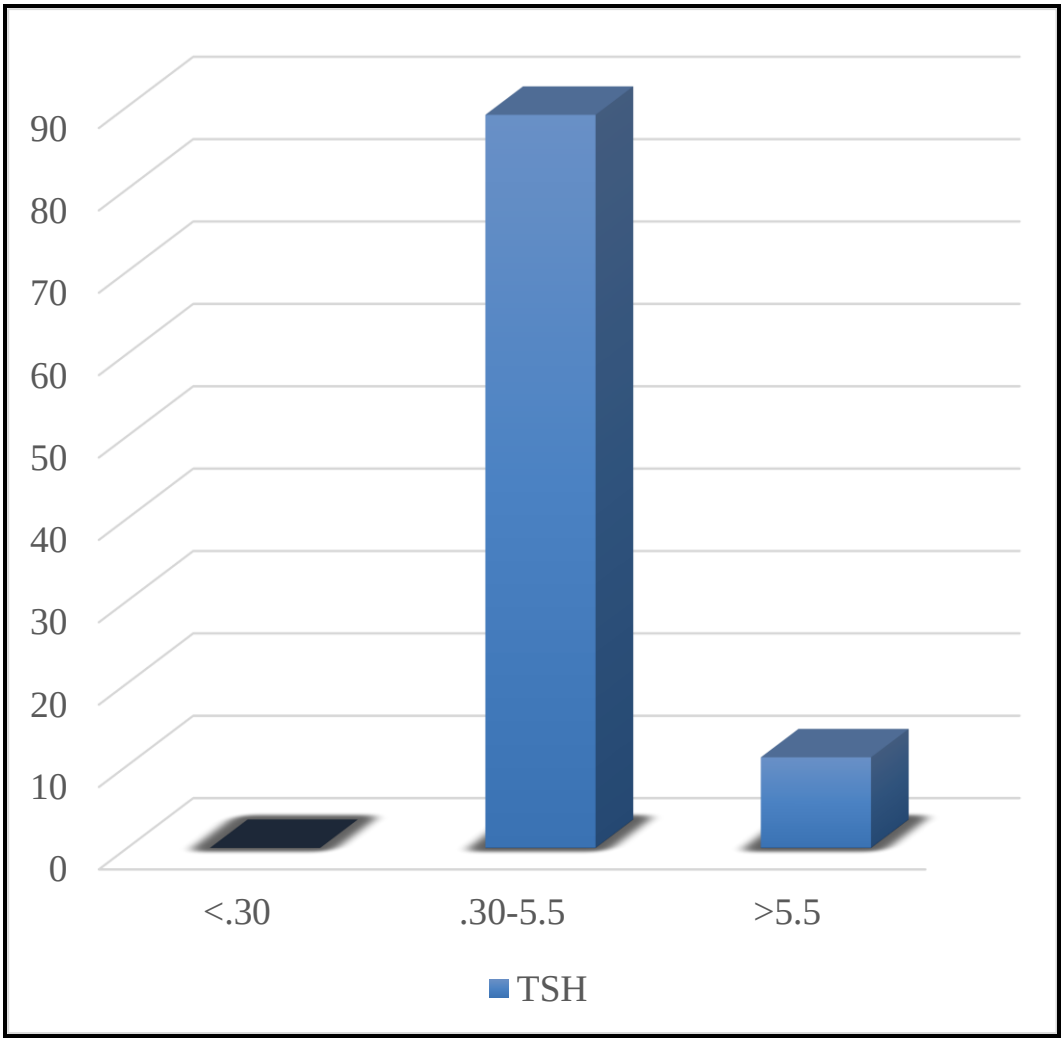
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	< 2	30	30.0	30.0	30.0
	2-5	60	60.0	60.0	90.0
	> 5	10	10.0	10.0	100.0
	Total	100	100.0	100.0	



Distribution of ART duration among study population. In our study group most of the patients ART duration under 2 to 5 years.

Table F: Free TSH distribution of studied patients

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Normal	89	89.0	89.0	89.0
	Abnormal	11	11.0	11.0	100.0
	Total	100	100.0	100.0	



TSH Distribution Among Studied Population Shows the Prevalence of Thyroid Dysfunction Is 11%

DESCRIPTIVE STATISTICS

Mean and standard deviation of variables study group.

	N	Minimum	Maximum	Mean	Std. Deviation
Free T3	100	1.0	3.2	2.106	.3290
Free T4	100	.6	1.5	1.012	.1896
TSH	100	.36	150.00	4.8026	14.79200
CD4 count	100	86	1619	501.46	262.302
Valid N (listwise)	100				

Mean CD4 and TSH in our study population is 501.46 and 4.80 respectively…

CORRELATIONS

Correlation between free T3, T4 , TSH with CD4 count.

		Free T3	Free T4	TSH	CD4 count
Free T3	Pearson Correlation	1	.231(*)	-.358(**)	.169
	Sig. (2-tailed)	.	.021	.000	.094
	N	100	100	100	100
Free T4	Pearson Correlation	.231(*)	1	-.234(*)	.120
	Sig. (2-tailed)	.021	.	.019	.236
	N	100	100	100	100
TSH	Pearson Correlation	-.358(**)	-.234(*)	1	-.173
	Sig. (2-tailed)	.000	.019	.	.086
	N	100	100	100	100
CD4 count	Pearson Correlation	.169	.120	-.173	1
	Sig. (2-tailed)	.094	.236	.086	.
	N	100	100	100	100

This table shows correlation between Free T3, Free T4, TSH with CD4 count. There is positive coreelation between free T3, T4,with CD4 count… and negatively correlates with TSH..

CROSS TABLES

Table 1: Relationship between Free T3 and CD4.

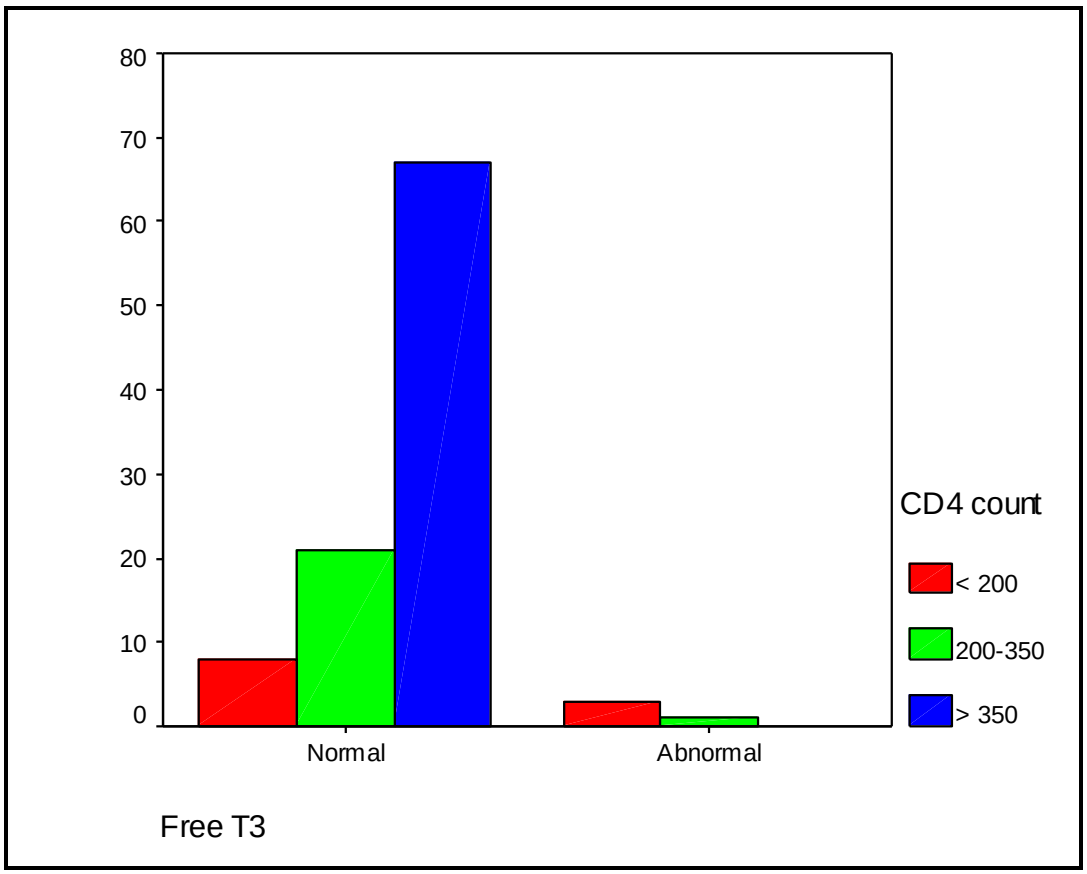
			CD4 count			Total
			< 200	200-350	> 350	
Free T3	Normal	Count	8	21	67	96
		% within Free T3	8.3%	21.9%	69.8%	100.0%
		% within CD4 count	72.7%	95.5%	100.0%	96.0%
	Abnormal	Count	3	1	0	4
		% within Free T3	75.0%	25.0%	.0%	100.0%
% within CD4 count		27.3%	4.5%	.0%	4.0%	
Total		Count	11	22	67	100
		% within Free T3	11.0%	22.0%	67.0%	100.0%
		% within CD4 count	100.0%	100.0%	100.0%	100.0%

CHI-SQUARE TESTS

	Value	Df	Asymp. Sig. (2-sided)
Pearson Chi-Square	18.324(a)	2	.000
Likelihood Ratio	12.562	2	.002
Linear-by-Linear Association	15.178	1	.000
N of Valid Cases	100		

Table 1 shows that low T3 patients have CD4 count less than 200 and pearson chi square significant Level is .000 and likely hood ratio is .002.

RELATIONSHIP BETWEEN FREE T3 AND CD4



.TABLE 2: RELATIONSHIP BETWEEN FREE T4 AND CD4

			CD4 count			Total
			< 200	200-350	> 350	
Free T4	Normal	Count	8	22	66	96
		% within Free T4	8.3%	22.9%	68.8%	100.0%
		% within CD4 count	72.7%	100.0%	98.5%	96.0%
	Abnormal	Count	3	0	1	4
		% within Free T4	75.0%	.0%	25.0%	100.0%
% within CD4 count		27.3%	.0%	1.5%	4.0%	
Total		Count	11	22	67	100
		% within Free T4	11.0%	22.0%	67.0%	100.0%
		% within CD4 count	100.0%	100.0%	100.0%	100.0%

CHI-SQUARE TESTS

	Value	Df	Asymp. Sig. (2-sided)
Pearson Chi-Square	17.529(a)	2	.000
Likelihood Ratio	10.303	2	.006
Linear-by-Linear Association	9.938	1	.002
N of Valid Cases	100		

Table 2 shows there is positive correlation between Free T4 and CD4 count, low T4 level patients are mostly have low CD4 count. Pearson chi square .000 and likely hood ratio .006

Relationship between Free T4 and CD4 count.

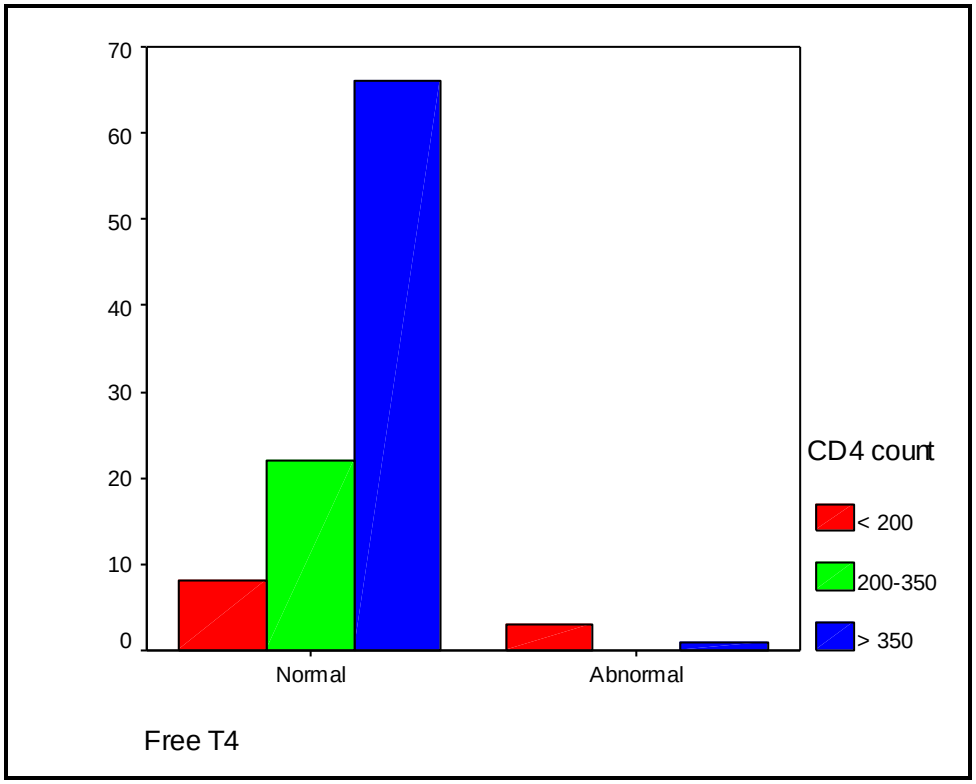


Table 3: Relationship between TSH and CD4.

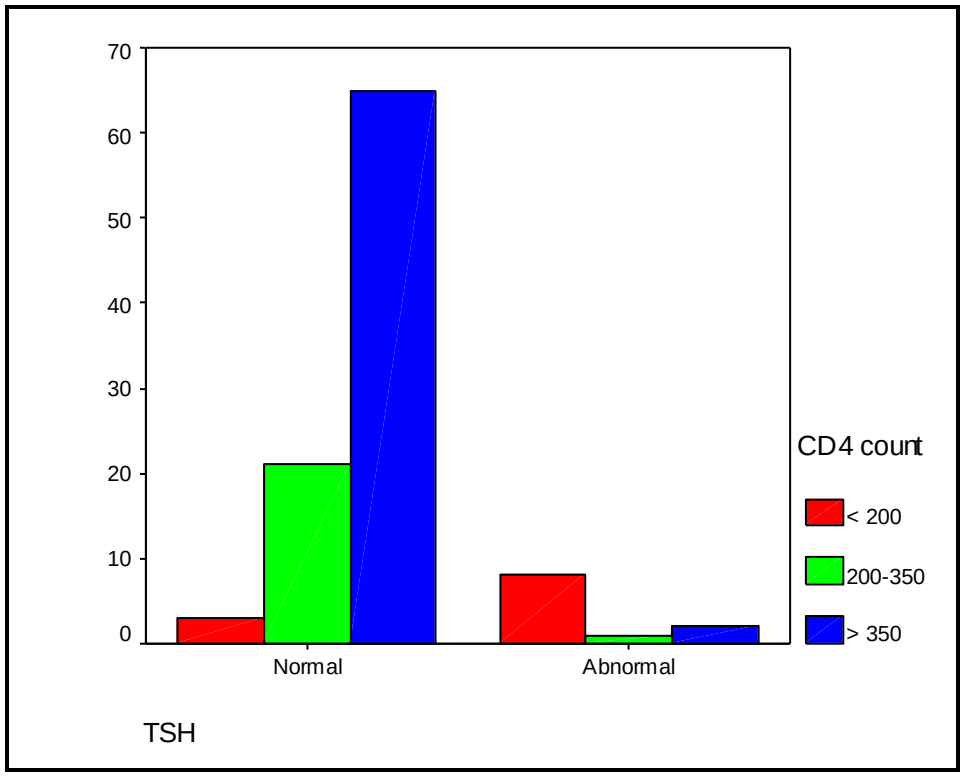
			CD4 count			Total
			< 200	200-350	> 350	
TSH	Normal	Count	3	21	65	89
	Abnormal	% within TSH	3.4%	23.6%	73.0%	100.0%
		% within CD4 count	27.3%	95.5%	97.0%	89.0%
		Count	8	1	2	11
	Count	% within TSH	72.7%	9.1%	18.2%	100.0%
		72.7%	4.5%	3.0%	11.0%	
% within CD4 count		11	22	67	100	
Total		% within TSH	11.0%	22.0%	67.0%	100.0%
		% within CD4 count	100.0%	100.0%	100.0%	100.0%

CHI-SQUARE TESTS

	Value	Df	Asymp. Sig. (2-sided)
Pearson Chi-Square	48.144(a)	2	.000
Likelihood Ratio	30.290	2	.000
Linear-by-Linear Association	32.060	1	.000
N of Valid Cases	100		

Table 3 shows there is negative correlation between TSH and CD4 count. Out of 11 abnormal[>5.5] TSH patients , 8 are have CD4 count <200.

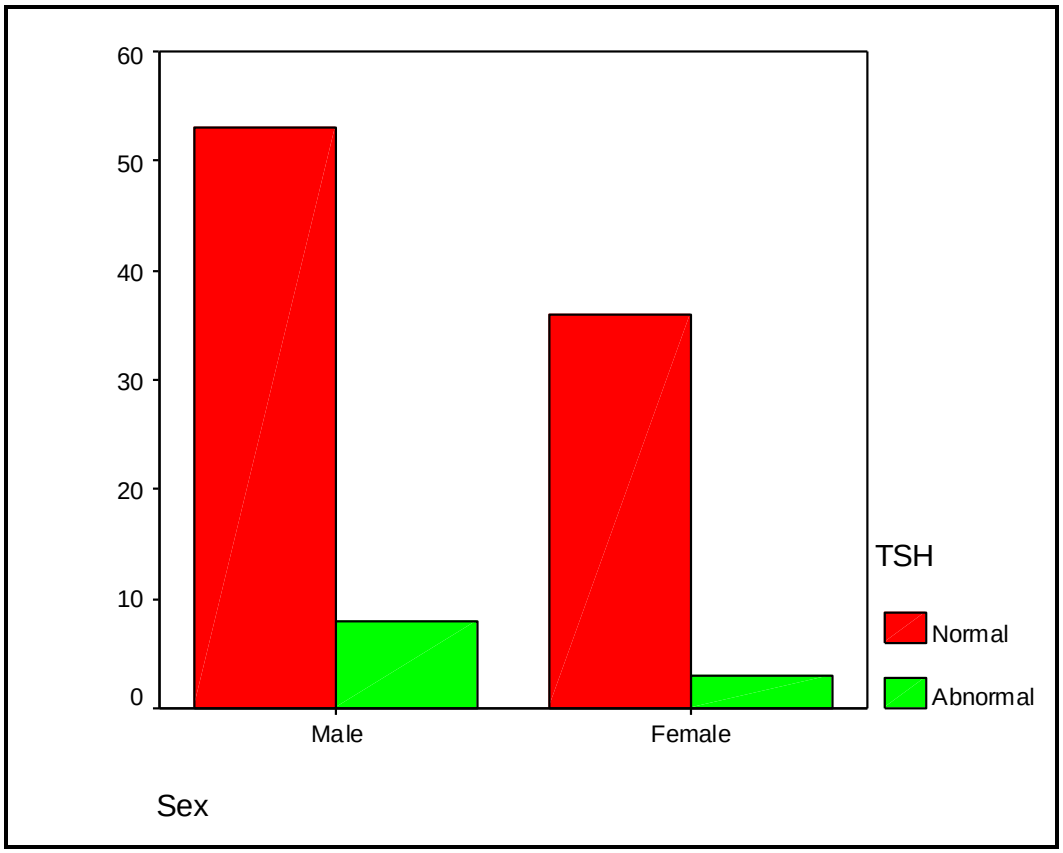
Pearson chi square significant at .ooo and liklyhood ratio is .000



Correlation between TSH and CD4 count.

CORRELATION BETWEEN SEX AND TSH COUNT.

Most of abnormal TSH level patients 13% are MALE sex..indicates that male sex is risk factor for thyroid dysfunction in HIV patients on ART.



Correlation Between Sex And TSH

Table 4

CORRELATION BETWEEN SEX AND CD4 COUNT

			CD4 count			Total
			< 200	**200-350**	**> 350**	
Sex	Male	Count	9	15	37	61
		% within Sex	14.8%	24.6%	60.7%	100.0%
		% within CD4 count	81.8%	68.2%	55.2%	61.0%
	Female	Count	2	7	30	39
		% within Sex	5.1%	17.9%	76.9%	100.0%
		% within CD4 count	18.2%	31.8%	44.8%	39.0%
Total		Count	11	22	67	100
		% within Sex	11.0%	22.0%	67.0%	100.0%
		% within CD4 count	100.0%	100.0%	100.0%	100.0%

CHI-SQUARE TESTS

	Value	Df	Asymp. Sig. (2-sided)
Pearson Chi-Square	3.421(a)	2	.181
Likelihood Ratio	3.648	2	.161
Linear-by-Linear Association	3.386	1	.066
N of Valid Cases	100		

CORRELATION BETWEEN SEX AND CD4 COUNT .

Table 4 shows that low CD4 count up to 14.8% are male sex.

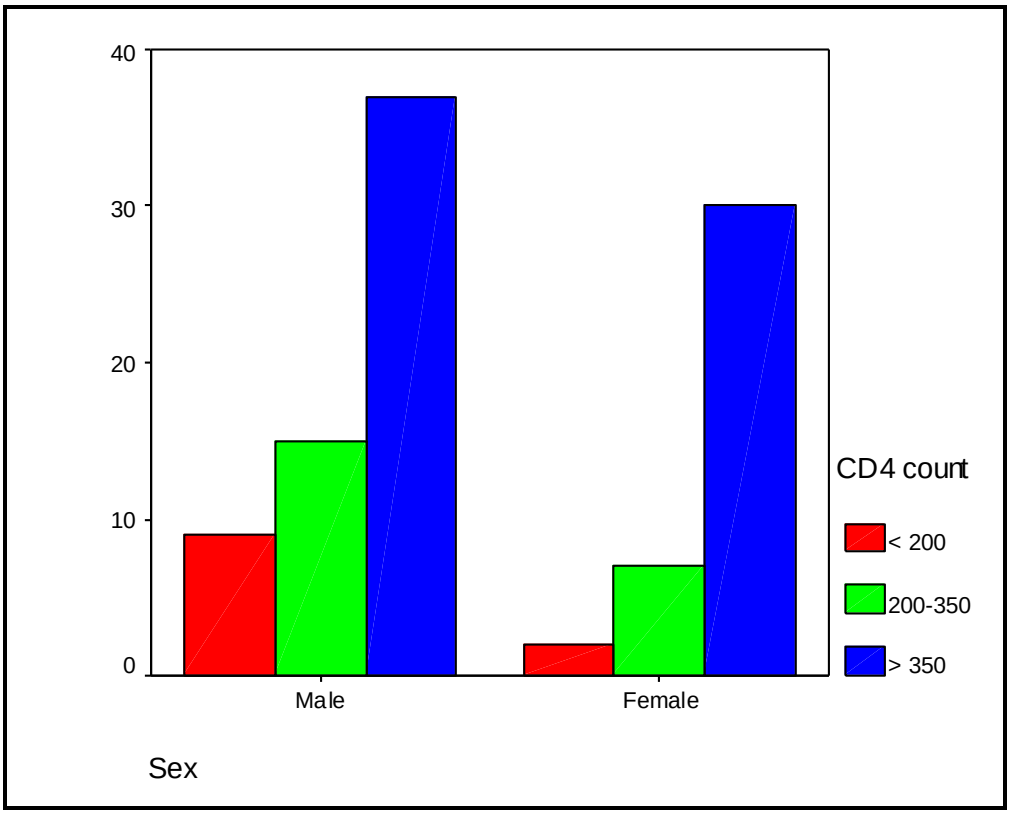


TABLE 5

CORRELATION BETWEEN STAGE OF HIV AND TSH LEVEL

			TSH		
			Normal	Abnormal	Total
Stage	I	Count	67	4	71
		% within Stage	94.4%	5.6%	100.0%
		% within TSH	75.3%	36.4%	71.0%
	II	Count	14	4	18
		% within Stage	77.8%	22.2%	100.0%
		% within TSH	15.7%	36.4%	18.0%
	III	Count	7	3	10
		% within Stage	70.0%	30.0%	100.0%
		% within TSH	7.9%	27.3%	10.0%
	IV	Count	1	0	1
		% within Stage	100.0%	.0%	100.0%
		% within TSH	1.1%	.0%	1.0%
Total		Count	89	11	100
		% within Stage	89.0%	11.0%	100.0%
		% within TSH	100.0%	100.0%	100.0%

CHI-SQUARE TESTS

	Value	Df	Asymp. Sig. (2-sided)
Pearson Chi-Square	8.215(a)	3	.042
Likelihood Ratio	7.235	3	.065
Linear-by-Linear Association	6.073	1	.014
N of Valid Cases	100		

The Table 5 shows that abnormal TSH seen in both early and late stage of disease course. In our study 8 patients are in stage 1& 2.. three patients are stage 3.

RELATION BETWEEN STAGE OF HIV AND TSH

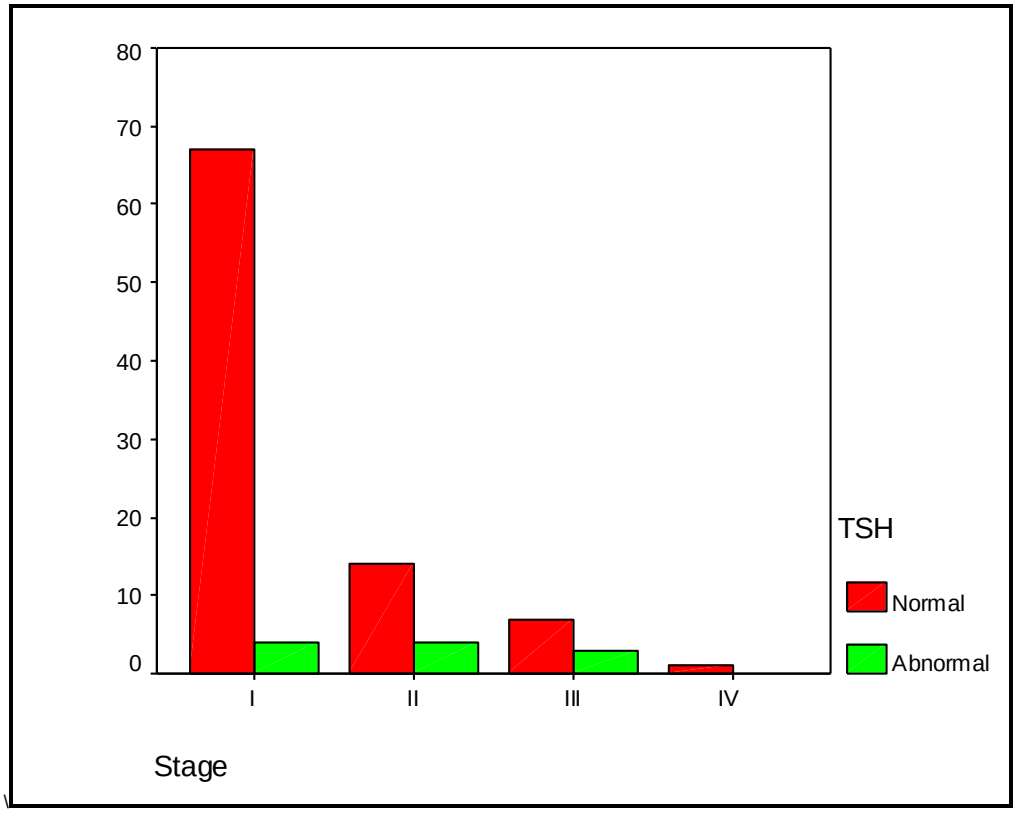


TABLE 6

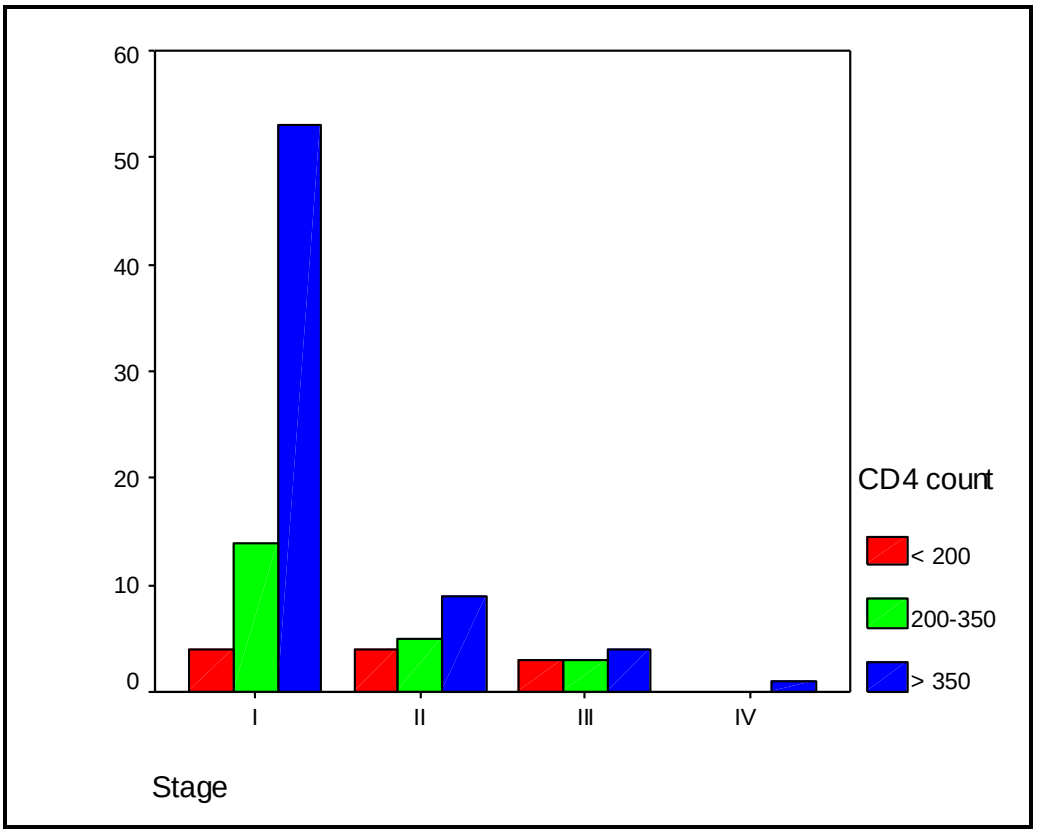
RELATION BETWEEN STAGE OF HIV AND CD4 COUNT

			CD4 count			Total
			< 200	200-350	> 350	
Stage	I	Count	4	14	53	71
		% within Stage	5.6%	19.7%	74.6%	100.0%
		% within CD4 count	36.4%	63.6%	79.1%	71.0%
	II	Count	4	5	9	18
		% within Stage	22.2%	27.8%	50.0%	100.0%
		% within CD4 count	36.4%	22.7%	13.4%	18.0%
	III	Count	3	3	4	10
		% within Stage	30.0%	30.0%	40.0%	100.0%
		% within CD4 count	27.3%	13.6%	6.0%	10.0%
	IV	Count	0	0	1	1
		% within Stage	.0%	.0%	100.0%	100.0%
		% within CD4 count	.0%	.0%	1.5%	1.0%
Total		Count	11	22	67	100
		% within Stage	11.0%	22.0%	67.0%	100.0%
		% within CD4 count	100.0%	100.0%	100.0%	100.0%

CHI-SQUARE TESTS

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	10.910(a)	6	.091
Likelihood Ratio	10.283	6	.113
Linear-by-Linear Association	7.103	1	.008
N of Valid Cases	100		

Table 6 shows that patients with CD4 count above 350 are mostly early stage [1 & 2] , and disease progressed the CD4 count falls significantly.



CORRELATION BETWEEN HIV STAGE AND CD4 COUNT.

TABLE 7

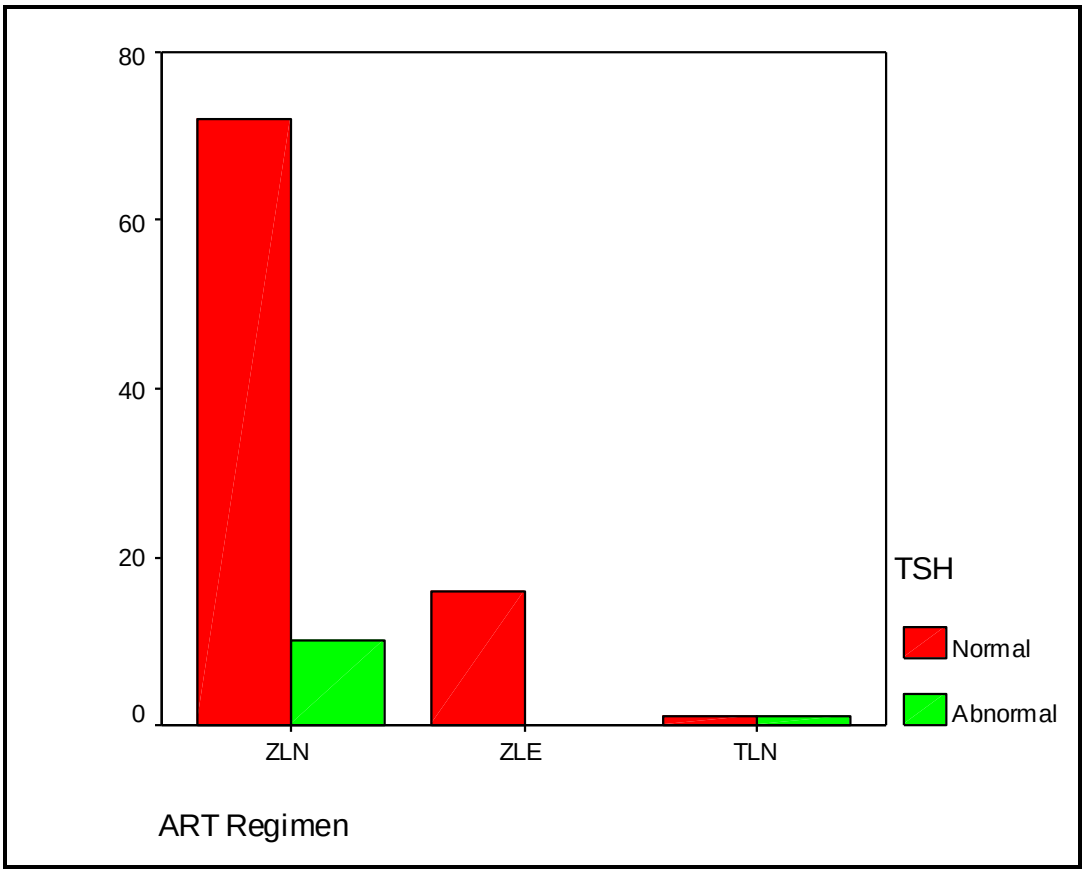
RELATION BETWEEN ART Regimen and TSH

			TSH		Total
			Normal	**Abnormal**	
ART Regimen	ZLN	Count	72	10	82
		% within ART Regimen	87.8%	12.2%	100.0%
		% within TSH	80.9%	90.9%	82.0%
	ZLE	Count	16	0	16
		% within ART Regimen	100.0%	.0%	100.0%
		% within TSH	18.0%	.0%	16.0%
	TLN	Count	1	1	2
		% within ART Regimen	50.0%	50.0%	100.0%
		% within TSH	1.1%	9.1%	2.0%
Total		Count	89	11	100
		% within ART Regimen	89.0%	11.0%	100.0%
		% within TSH	100.0%	100.0%	100.0%

CHI-SQUARE TESTS

	Value	Df	Asymp. Sig. (2-sided)
Pearson Chi-Square	5.204(a)	2	.074
Likelihood Ratio	5.720	2	.057
Linear-by-Linear Association	.020	1	.887
N of Valid Cases	100		

Table 7 shows that most of abnormal TSH patients are under ZLN regimen .but It is not statistically significant.



COREELATION BETWEEN ART REGIMEN AND TSH

TABLE 8

ART Regimen and CD4 count

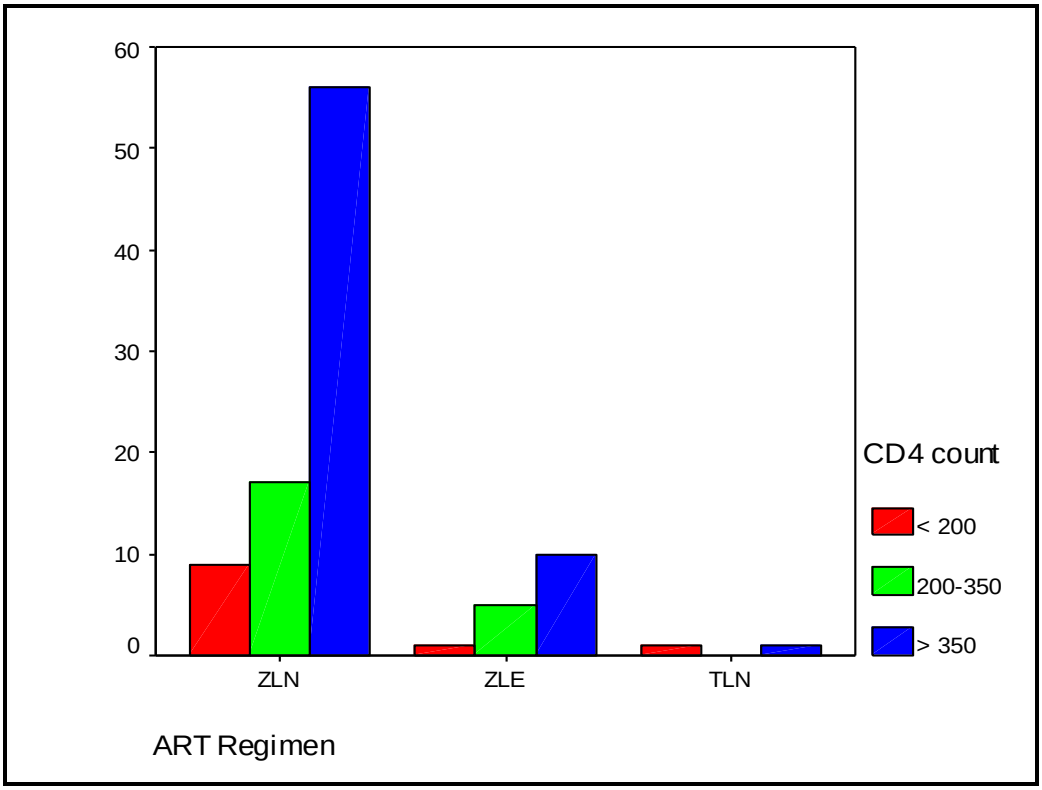
Crosstab

			CD4 count			Total
			< 200	200-350	> 350	
ART Regimen	ZLN	Count	9	17	56	82
		% within ART Regimen	11.0%	20.7%	68.3%	100.0%
		% within CD4 count	81.8%	77.3%	83.6%	82.0%
	ZLE	Count	1	5	10	16
		% within ART Regimen	6.3%	31.3%	62.5%	100.0%
		% within CD4 count	9.1%	22.7%	14.9%	16.0%
	TLN	Count	1	0	1	2
		% within ART Regimen	50.0%	.0%	50.0%	100.0%
		% within CD4 count	9.1%	.0%	1.5%	2.0%
Total		Count	11	22	67	100
		% within ART Regimen	11.0%	22.0%	67.0%	100.0%
		% within CD4 count	100.0%	100.0%	100.0%	100.0%

CHI-SQUARE TESTS

	Value	Df	Asymp. Sig. (2-sided)
Pearson Chi-Square	4.371(a)	4	.358
Likelihood Ratio	3.513	4	.476
Linear-by-Linear Association	.514	1	.474
N of Valid Cases	100		

Table 8 shows that most of patients are ZLN regimen [82%], ZLE [16%], TLN [2%] … 9 patients with low CD4 count are in ZLN regimen.



Correlation Between Cd4 Count And Art Regimen.

TABLE 9

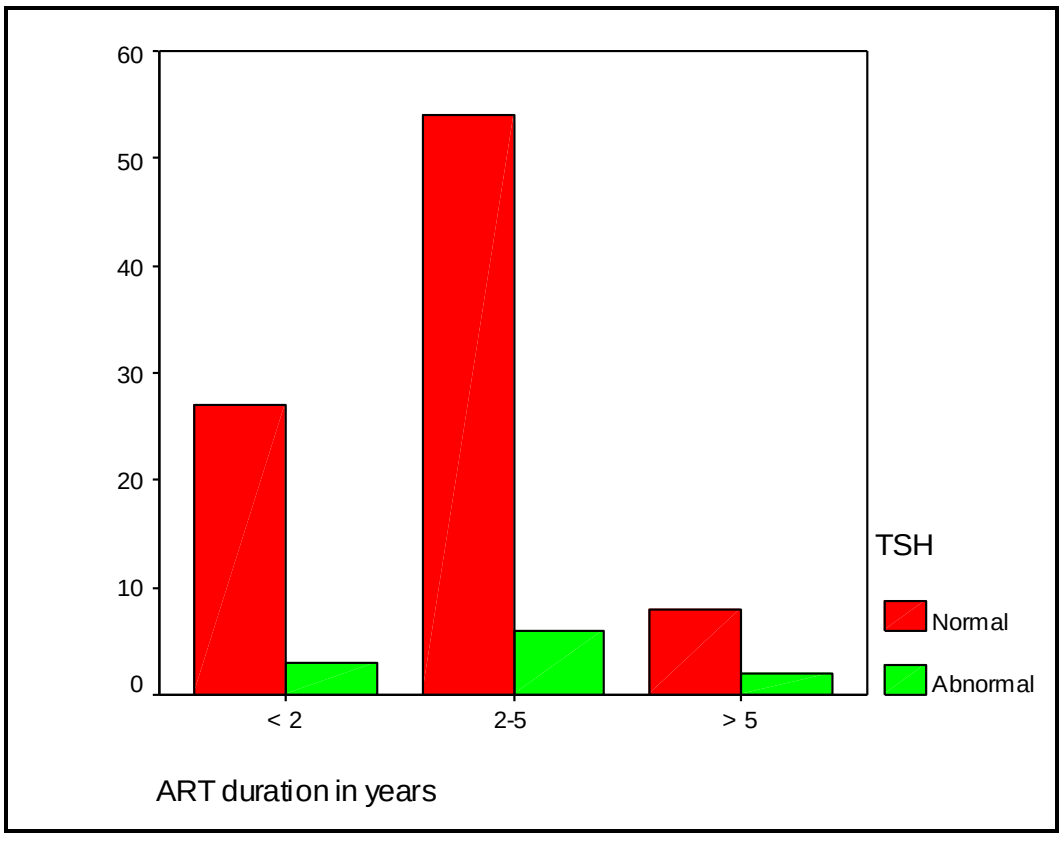
ART duration in years and TSH

			TSH		Total
			Normal	**Abnormal**	
ART duration in years	< 2	Count	27	3	30
		% within ART duration in years	90.0%	10.0%	100.0%
		% within TSH	30.3%	27.3%	30.0%
	2-5	Count	54	6	60
		% within ART duration in years	90.0%	10.0%	100.0%
		% within TSH	60.7%	54.5%	60.0%
	> 5	Count	8	2	10
		% within ART duration in years	80.0%	20.0%	100.0%
		% within TSH	9.0%	18.2%	10.0%
Total		Count	89	11	100
		% within ART duration in years	89.0%	11.0%	100.0%
		% within TSH	100.0%	100.0%	100.0%

CHI-SQUARE TESTS

	Value	Df	Asymp. Sig. (2-sided)
Pearson Chi-Square	.919(a)	2	.632
Likelihood Ratio	.780	2	.677
Linear-by-Linear Association	.404	1	.525
N of Valid Cases	100		

Table 9 shows that increasing ART duration leads to more changes in thyroid function. In our study 6 patients with abnormal TSH are ART duration 2 – 5 years. .but it is statistically not significant.



Correlation between ART duration and CD4 count.

TABLE 10

ART DURATION IN YEARS AND CD4 COUNT

Crosstab

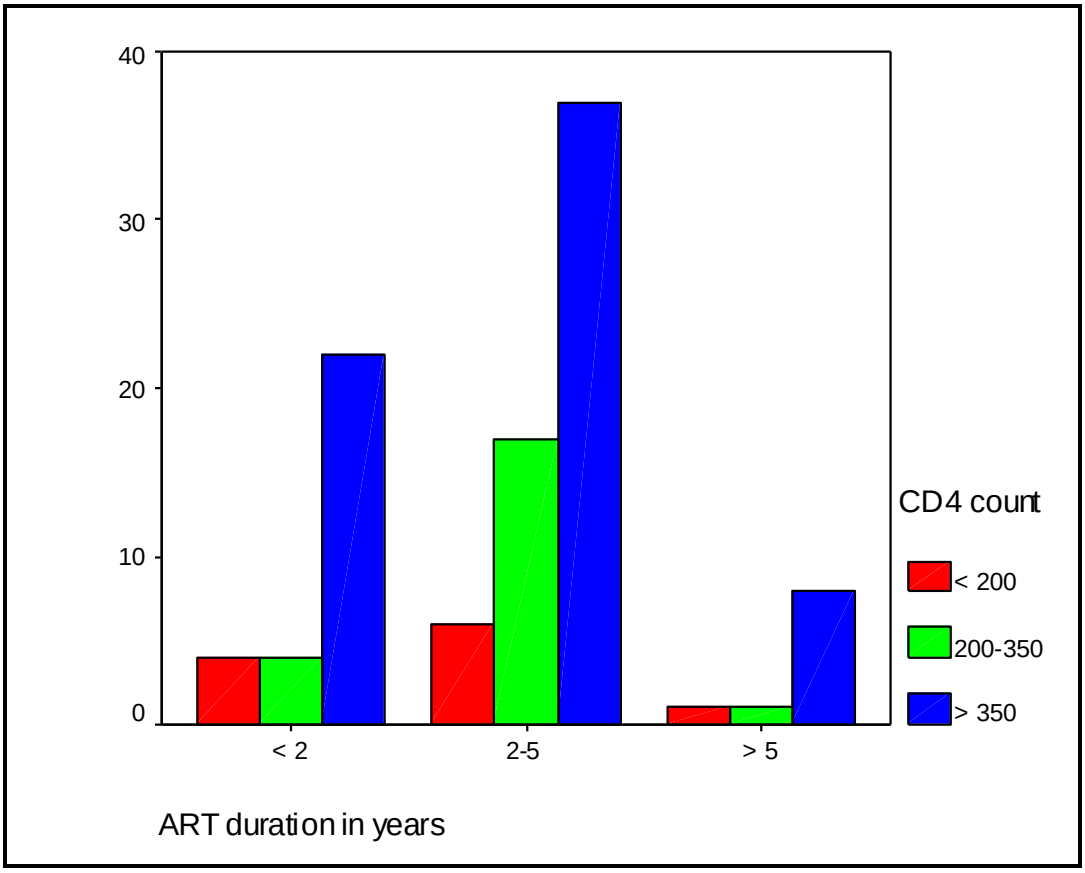
			CD4 count			Total
			< 200	**200-350**	**> 350**	
ART duration in years	< 2	Count	4	4	22	30
		% within ART duration in years	13.3%	13.3%	73.3%	100.0%
		% within CD4 count	36.4%	18.2%	32.8%	30.0%
	2-5	Count	6	17	37	60
		% within ART duration in years	10.0%	28.3%	61.7%	100.0%
		% within CD4 count	54.5%	77.3%	55.2%	60.0%
	> 5	Count	1	1	8	10
		% within ART duration in years	10.0%	10.0%	80.0%	100.0%
		% within CD4 count	9.1%	4.5%	11.9%	10.0%
Total		Count	11	22	67	100
		% within ART duration in years	11.0%	22.0%	67.0%	100.0%
		% within CD4 count	100.0%	100.0%	100.0%	100.0%

CHI-SQUARE TESTS

	Value	Df	Asymp. Sig. (2-sided)
Pearson Chi-Square	3.671(a)	4	.452
Likelihood Ratio	3.897	4	.420
Linear-by-Linear Association	.002	1	.961
N of Valid Cases	100		

Table 10 shows that ART duration more than 2 years patients have CD4 count above 350 in most of study populatin.

RELATION BETWEEN ART DURATION AND CD4 COUNT



DISCUSSION

- In this cross sectional study conducted in Rajiv Gandhi government general hospital, institute of internal medicine Chennai over 3 month period from April to September among 100 adult hiv patients on anti retroviral therapy.

- The study group population subjected to clinical examination and biochemical test thyroid profile and cd4 count, variables are analyzed by appropriate statistical method.

- The age distribution in our study group 51% of patients are 18 to 39 years, 48% in 40 to 59 years age group and male sex 61% , female 39% in this study group.[Table A and B]

- In our study most of patients 71% are in WHO clinical stage 1, and 18% patients in stage 2, only 10% of patients in stage 3 [Table C].

- In the study group most of patients 82% under ZLN regimen, 16% are in ZLE regimen[Table D], and 60% patiets on ART about 2 to 5 year duration, 30% less

than 2 year, only 5% patients >5 year duration of therapy.[Table E]

- Thyroid dysfunction in our study group is
  - Prevalence - 11 %
  - Overt hypothyroidism - 2 %
  - Sub clinical hypothyroidism - 9 %
- Isolated low T4 level in our study group is 4%.
- In Beltran et al the prevalence of thyroid dysfunction is
  - Overt hypothyroidism - 2.6%
  - Sub clinical hypothyroidism - 6.6%
  - Isolated low T4 level - 6.8%
- In this study group the mean values are
  - Free T3 - 2.106 with SD.3290
  - Free T4 - 1.01`2 with SD .1896
  - Tsh - 4.80 with SD 14.79

- CD4 count - 501.46 with SD 262 .30

- There is positive correlation between Free T3 and CD4 count in our study that is statistically significant.[Table 1]
  - Pearson chi square - .000
  - Likely hood ratio - .002
  - Linear by linear association - .000
- Also Free T4 Positively correlates with CD4 count which is statistically significant.[Table 2]
  - Pearson chi square - .000
  - Likely hood ratio - .006
  - Linear by linear association - .002
- In this study group , 11 patients have abnormal TSH > 5.5, among these , 8 patient CD4 count < 200 , and 1 patient 200 - 350 , 2 patients are >350.
- Indicates that the thyroid dysfunction common in patients with low CD4 count.[Table 3]

- Statistically significant correlation seen in our study
  - Pearson chi square - .000
  - Likely hood ratio - .000
  - Linear by linear association - .000
- Among these 6 patients are age group 40 to 59 years, and 5 18 t0 39 years . and 8 patients are male, 3 female patients.
- Indicates that thyroid dysfunction common in male sex and older age group.
- Among these patients with abnormal TSH , 10 patients on ZLN regimen, 1 patient TLN regimen and 6 patients on medication 2 to 5 years duration.
- Indicates that thyroid dysfunction common in patients with ZLN regimen and longer duration of ART.
- In these 11 patients, stage 1 disease 4 patients, stage 2 in 4 patients , stage 3 in 3 patients. [Table 5]
- Indicates that thyroid dysfunction common in both early and late stage of disease.

Various other studies shows that

- Calza et al

  Sub clinical hypothyroidism 12.2%

- German study

  Sub clinical hypothyroidism 17.4%

- French study

  sub clinical hypothyroidism 8.5%

  overt hypothyroidism 1.9%.

CONCLUSION

- We conclude from our study , there is increased prevalence of thyroid dysfunction among HIV infected patients especially on anti retro viral therapy.

- There is significant correlation between TSH and CD4 count found in our study .. TSH negatively correlates and T3 , T4 positively correlates with CD4 count.

- The most patients with thyroid dysfunction are associated with low CD4 count, longer duration of ART, ZLN regimen , and in age group 40 - 59 years.

- The study concludes the risk factor for thyroid dysfunction in HIV patients male sex, low CD4 count, patient on ART, longer disease course.

- The study also shows that the prevalence of thyroid dysfunction common in both early and late stage of disease.

- By this study report that screening indicated in symptomatic patients and HIV patients on ART with above risk factor. And screening of asymptomatic HIV patients recommendations need further large study.

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ABBREVIATIONS

HIV	Human immuno deficiency virus
AIDS	Acquired immuno deficiency syndrome
HAART	Highly active anti retro viral therapy
TFT	Thyroid function test
TSH	Thyroid stimulating hormone
CMV	Cytomegalovirus
NACO	National AIDS control organization
WHO	World health organization
MAC	Mycobacterium avium intercellular complex
ELISA	Enzyme linked immuno sorbent assay
PCR	Polymerase chain reaction
NNRTI	Non - Nucleoside reverse transcriptase inhibitor
NRTI	Nucleoside reverse transcriptase inhibitor.
TB	Tuberculosis
NVP	Nevirapine
TDF	Tenofovir
ATT	Anti tuberculous therapy
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HSV	Herpes simplex virus

PROFORMA

Name :

Age :

Sex :

Ip / op no :

Date :

Place :

SYMPTOMS QUESTIONNAIRE

Constipation	-	+ / -
Fatigability	-	+/-
Weight gain	-	+/-
Cold intolerance	-	+/-
Heat intolerance	-	+/-
Tremor	-	+/-
Weight loss	-	+/-

ART regimen -

ART duration -

WHO stage -

CLINICAL EXAMINATION

Blood pressure -

Heart rate -

Pallor -

Thyromegaly -

BIOCHEMICAL PARAMETERS:

Free T3 -

Free T4 -

Tsh -

CD4 count -

S. No	Hospital No:	Age	Sex	WHO stage	ART regimen	ART duration	dry skin	costipation	Cold intolerance	tremors	heat intolerance	weight gain	Thromegay	Weight loss	Free T3	Free T4	TSH	CD4 count
1	1285	2	1	1	1	1	1	2	2	2	2	2	2	1	1.8	1.2	1.29	244
2	3216	1	2	2	1	2	2	2	2	2	2	2	2	2	2.2	0.8	0.83	806
3	302	1	2	1	1	3	1	2	2	2	2	1	2	2	2.1	1	7.4	648
4	3759	2	1	1	1	1	1	2	2	2	2	2	2	2	2.3	1.3	1.32	513
5	2392	2	1	3	2	2	2	2	2	2	2	2	2	2	1.4	1	4.25	243
6	1427	1	2	1	1	2	2	2	2	2	2	2	2	2	2.6	0.8	2.57	608
7	3821	1	1	3	1	1	2	1	2	2	2	2	2	2	2.5	1.2	1.75	291
8	4741	2	1	2	1	2	2	2	2	2	2	2	2	1	1.9	0.78	6.97	167
9	288	1	1	2	1	3	2	2	2	2	2	2	2	2	1.8	1.4	1.74	397
10	134	1	2	1	1	3	2	2	2	2	2	2	2	2	2.3	1.2	4.25	403
11	84722	1	2	3	1	2	2	1	1	2	2	2	2	2	1.9	0.9	8.5	94
12	3362	2	2	1	1	1	2	2	2	2	2	2	2	2	2.2	1	1.47	718
13	4348	1	2	1	1	1	2	2	2	2	2	2	2	2	2.4	0.7	3.16	661
14	1447	2	1	1	2	1	2	2	2	2	2	2	2	2	2	0.85	4.75	115
15	4058	2	1	3	3	1	1	2	2	2	2	2	2	1	2.6	1.1	5.6	163
16	143/05	1	1	1	1	3	2	2	2	2	2	2	2	2	2.7	1.01	1.9	483
17	4028	1	1	1	1	1	2	2	2	2	2	2	2	1	2.8	0.88	1.71	727
18	2210	1	2	4	3	2	1	2	2	2	2	2	2	1	3.2	1.2	1.62	635
19	1733	3	1	1	2	1	2	2	2	2	2	2	2	2	2.5	1.06	2.54	509
20	2350	1	1	1	1	2	2	2	2	2	2	2	2	2	2.3	1.25	3.34	551
21	981/06	2	1	1	1	2	2	2	2	2	2	2	2	1	3.2	1.08	6.36	102
22	4221	2	1	2	1	2	2	2	2	2	2	2	2	1	2.4	0.78	1.95	116
23	1162	2	1	2	2	2	2	2	2	2	2	2	2	2	2.2	0.87	3.86	331
24	964	2	1	1	2	2	2	2	2	2	2	2	2	2	2	0.99	4.4	562
25	3432	2	1	1	2	2	2	2	2	2	2	2	2	1	1.9	0.91	1.48	1130
26	954	1	1	1	1	2	1	2	2	2	2	2	2	1	2	0.87	1.29	336
27	4135	1	1	1	1	2	2	2	2	2	2	2	2	2	2.1	0.95	4.99	697
28	2194	1	2	1	1	2	2	2	2	2	2	2	2	2	2	1.06	5.26	350
29	4263	1	1	1	1	1	2	2	2	2	2	2	2	2	1.6	0.68	4.94	86
30	4074	1	1	1	2	1	1	2	2	2	2	2	2	2	2.1	0.88	1.65	451
31	8516	1	1	2	1	1	1	2	2	2	2	2	2	1	2	0.91	6.88	143
32	92506	2	1	1	1	1	1	2	2	2	2	2	2	1	2.16	1.12	7.43	865
33	4830	2	1	1	1	1	2	2	2	2	2	2	2	2	1.9	0.86	3.41	387
34	1949	1	1	1	1	2	2	2	2	2	2	2	2	2	2	0.82	2.98	573
35	5706	1	2	1	2	2	2	2	2	2	2	2	2	2	2.6	1.05	1.42	1619
36	2719	1	2	1	1	2	2	2	2	2	2	2	2	2	2	0.76	4.68	371

S. No	Hospital No:	Age	Sex	WHO stage	ART regimen	ART duration	dry skin	costipation	Cold intolerance	tremors	heat intolerance	weight gain	Thromegay	Weight loss	Free T3	Free T4	TSH	CD4 count
37	4272	2	1	1	1	1	2	2	2	2	2	2	2	2	1.9	0.91	2.26	550
38	2371	2	2	1	1	2	2	2	2	2	2	2	2	2	2.4	0.83	2.08	730
39	971	1	1	1	1	2	2	2	2	2	2	2	2	2	2.2	0.95	1.71	936
40	1936	1	2	1	1	2	2	2	2	2	2	2	2	2	2.4	0.78	1.71	335
41	2318	2	1	1	1	2	2	2	2	2	2	2	2	2	1.8	0.93	3.07	505
42	3448	1	2	2	1	2	1	1	1	2	2	1	1	2	1	0.61	150	165
43	2321	1	2	1	2	1	2	2	2	2	2	2	2	2	1.9	0.77	3.09	517
44	2726	1	2	1	2	1	2	2	2	2	2	2	2	2	1.9	0.85	1.91	1278
45	2502	1	1	1	1	2	2	2	2	2	2	2	2	2	1.8	1.09	0.36	539
46	2503	1	2	1	1	2	2	2	2	2	2	2	2	2	2.1	1.06	1.66	653
47	3343	2	1	1	1	1	2	2	2	2	2	2	2	2	2.2	1.09	4.66	601
48	2691	1	2	1	1	1	2	2	2	2	2	2	2	2	2.1	1.08	1.93	855
49	3628	1	1	1	1	2	2	2	2	2	2	2	2	1	1.9	0.91	3.58	276
50	3281	1	2	1	1	2	2	2	2	2	2	2	2	2	2.2	1.07	2.73	948
51	681	2	1	1	1	2	2	2	2	2	2	2	2	2	1.9	0.96	4.49	528
52	3059	2	1	1	1	2	2	2	2	2	2	2	2	2	2	1.17	3.5	435
53	3420	1	1	1	1	1	2	2	2	2	2	2	2	2	2.2	1.25	3.5	453
54	3434	2	1	1	1	2	2	2	2	2	2	2	2	2	2	1.14	2.25	506
55	1547	1	1	1	1	2	2	2	2	2	2	2	2	2	2.4	1.25	2.38	712
56	2859	1	1	1	1	2	1	2	2	2	2	2	2	1	1.8	0.9	9.21	155
57	3308	1	1	2	1	1	2	2	2	2	2	2	2	2	2.1	1.13	1.43	336
58	2364	1	1	2	1	1	2	2	2	2	2	2	2	2	2.3	1.1	2.6	497
59	3860	2	2	3	2	1	2	2	2	2	2	2	2	2	2.4	1.2	4.5	501
60	1068	2	1	1	1	2	2	2	2	2	2	2	2	2	2.4	0.88	3.73	369
61	2077	2	1	1	1	2	2	2	2	2	2	2	2	2	2.4	0.9	2.36	559
62	1337	2	2	1	1	2	2	2	2	2	2	2	2	2	1.9	1.2	3.1	507
63	114	2	2	1	1	2	2	2	2	2	2	2	2	2	2.1	1.12	2.5	502
64	2469	1	2	1	1	2	2	2	2	2	2	2	2	2	2.2	1.3	3.25	750
65	5247	1	2	1	1	2	2	2	2	2	2	2	2	2	2	0.99	3.64	992
66	3820	1	2	1	1	1	2	2	2	2	2	2	2	1	2.4	1.01	2.95	558
67	3759	2	2	1	1	2	2	2	2	2	2	2	2	2	2	0.7	2.85	653
68	1739	1	1	2	1	1	2	2	2	2	2	2	2	2	2.6	1.25	1.43	576
69	2502	1	1	1	1	2	2	2	2	2	2	2	2	2	2	1.07	2.1	326
70	2182	2	1	1	1	2	2	2	2	2	2	2	2	2	2	1.13	2.04	226
71	3077	2	1	2	1	2	2	2	2	2	2	2	2	2	1.8	1	6.25	256
72	4786	2	1	3	1	3	1	1	2	2	2	2	1	2	1.5	0.69	12.5	164

S. No	Hospital No:	Age	Sex	WHO stage	ART regimen	ART duration	dry skin	costipation	Cold intolerance	tremors	heat intolerance	weight gain	Thromegay	Weight loss	Free T3	Free T4	TSH	CD4 count
73	5660	2	1	3	2	3	2	2	2	2	2	2	2	1	2.1	0.6	2.75	456
74	7831	1	2	1	1	2	2	2	2	2	2	2	2	2	2.4	1	4.49	384
75	9201	2	2	2	2	2	2	2	2	2	2	2	2	2	2.2	0.9	4.5	208
76	1810	2	1	1	1	2	2	2	2	2	2	2	2	1	1.9	0.99	3.3	226
77	2378	2	1	3	2	3	1	2	2	2	2	2	2	1	1.8	1.2	1.5	289
78	4565	2	1	1	1	2	2	2	2	2	2	2	2	1	1.9	0.96	2.25	314
79	4400	1	2	1	1	1	2	2	2	2	2	2	2	2	1.86	1.24	2.5	336
80	5491	1	1	1	1	2	2	2	2	2	2	2	2	2	1.7	0.92	3.39	467
81	3322	1	2	1	1	2	2	2	2	2	2	2	2	2	1.96	0.8	2.35	512
82	1061	1	2	2	1	2	2	2	2	2	2	2	2	2	1.84	0.89	5.2	567
83	387	2	2	2	1	2	1	2	2	2	2	2	2	2	1.94	1.2	4.48	613
84	7700	2	1	2	1	3	2	2	2	2	2	2	2	2	2.25	1.25	4.56	436
85	1745	2	1	1	1	3	2	2	2	2	2	2	2	2	2.4	1.3	3.8	520
86	7432	2	1	1	2	2	2	2	2	2	2	2	2	2	1.85	0.8	2.5	560
87	8765	2	2	2	2	2	2	2	2	2	2	2	2	2	1.9	1.2	1.25	317
88	9123	1	2	1	1	1	2	2	2	2	2	2	2	2	1.7	1.45	2.26	846
89	6987	1	1	1	1	1	1	2	2	2	2	2	2	2	1.96	0.85	3.17	870
90	4671	2	1	1	1	2	2	2	2	2	2	2	2	2	2.25	1.2	3.3	396
91	7209	2	1	2	1	2	2	2	2	2	2	2	2	2	2.4	1.36	4.5	436
92	987	2	2	3	1	3	2	2	2	2	2	2	2	2	2.32	1.4	4.26	900
93	1004	2	1	2		1	2	2	2	2	2	2	2	2	1.7	0.9	2.23	746
94	4207	2	1	1	1	2	1	2	2	2	2	2	2	2	1.99	0.96	2.73	336
95	4090	1	2	1	1	2	2	2	2	2	2	2	2	2	2.26	1.12	3.5	350
96	2333	1	2	1	1	2	2	2	2	2	2	2	2	2	2.4	0.89	2.38	342
97	4212	1	1	1	1	2	1	2	2	2	2	2	2	1	1.92	0.96	1.96	286
98	1992	2	2	1	1	2	2	2	2	2	2	2	2	2	2.23	0.98	2.1	547
99	3089	2	2	1	1	1	2	2	2	2	2	2	2	2	1.9	1.46	2.38	602
100	4781	2	1	3	1	2	2	2	2	2	2	2	2	2	1.7	0.9	3.42	740

KEY TO MASTER CHART

AGE GROUP

- 18 to 39 yrs - 1
- 40 to 59 yrs - 2
- > 60 yrs - 3

SEX

- MALE - 1
- FEMALE - 2

WHO CLINICAL STAGE

- STAGE 1 - 1
- STAGE 2 - 2
- STAGE 3 - 3
- STAGE 4 - 4

ART DURATION

- < 2 yrs - 1
- 2 to 5 yrs - 2
- > 5 yrs - 3

ART REGIMEN

- ZLN - 1
- ZLE - 2
- TLN - 3

SYMPTOMS

- Present - 1
- Absent - 2

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI-3

EC Reg No.ECR/270/Inst./TN/2013
Telephone No : 044 25305301
Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr. P. Karthik,
Post Graduate, MD (General Medicine)
Institute of Internal Medicine,
Madras Medical College,
Chennai – 600003.

Dear Dr. P. Karthik,

The Institutional Ethics Committee has considered your request and approved your study titled **"PREVALENCE OF THYROID DYSFUNCTION IN HIV ADULT PATIENTS ON HIGHLY ACTIVE ANTI-RETROVIRAL THERAPY IRRESPECTIVE OF STAGING AND CORRELATION BETWEEN TSH AND CD4 COUNT"** No. 53072014.

The following members of Ethics Committee were present in the meeting held on 01.07.2014 conducted at Madras Medical College, Chennai-3.

1.	Dr. C. Rajendran, M.D.	-- Chairperson
2.	Dr. R. Vimala, M.D., Dean, MMC, Ch-3.	-- Deputy Chair Person
3.	Prof. Kalaiselvi, MD., Vice-Principal, MMC, Ch-3	-- Member Secretary
4.	Prof. Nandhini, M.D. Inst. of Pharmacology, MMC, Ch-3.	-- Member
5.	Dr. G. Muralidharan, Director Incharge , Inst. of Surgery	-- Member
6.	Prof. Md Ali, MD., DM., Prof & HOD of MGE, MMC, Ch-3.	-- Member
7.	Prof. Ramadevi, Director i/c, Biochemistry, MMC,Ch-3.	-- Member
8.	Prof. Saraswathy, MD., Director, Pathology, MMC, Ch-3.	-- Member
9.	Prof. Tito, Director, i/c. Inst. of Internal Medicine, MMC	-- Member
10.	Thiru. Rameshkumar, Administrative Officer	-- Lay Person
11.	Thiru. S. Govindasamy, BABL, High Court, Chennai-1.	-- Lawyer
12.	Tmt. Arnold Saulina, MA MSW	-- Social Scientist

We approve the proposal to be conducted in its presented form.

Sd/Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003

INFORMATION SHEET

TITLE:

We are conducting a study on "**PREVALENCE OF THYROID DYSFUNCTION IN ADULT HIV PATIENT ON HIGHLY ACTIVE ANTI-RETROVIRAL THERAPY IRRESPECTIVE OF STAGING & CORRELATION BETWEEN TSH AND CD4 COUNT"** among patients attending Rajiv Gandhi Government General Hospital ,Chennai and for that your specimen may be valuable to us.

NAME OF THE INVESTIGATOR: DR.P.KARTHIK.

THE STUDY:

To address the Thyroid dysfunction in adult hiv patient on highly active anti-retroviral therapy irrespective of staging & correlation between tsh and CD4 count.

STUDY DESIGN: Cross Sectional Study.

STUDY PROCEDURE

We are selecting certain cases and if you are found eligible, after filling up the questionnaires ,we may be using your blood samples to do special studies which Includes free T3, free T4, Thyroid stimulating hormone ,CD4 count. These tests in anyway do not affect your final report or management.

POSSIBLE RISKS:

No possible risks by means of this study.

POSSIBLE BENEFIT

If this study confirms the association , therapeutic intervention by means of supplementation of thyroxine can be considered.

The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled.

The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Signature of Investigator **Signature of Participant**

Date :
Place :

PATIENT CONSENT FORM

Study Detail : "Prevalence of thyroid dysfunction in adult hiv patient on highly active anti-retroviral therapy irrespective of staging & correlation between TSH and CD4 count"

Study Centre : Rajiv Gandhi Government General Hospital, Chennai.

Patient's Name :

Patient's Age :

Identification Number :

Patient may check (√) these boxes

a) I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction. ☐

b) I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected. ☐

c) I understand that sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study. ☐

d) I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well being or any unexpected or unusual symptoms. ☐

e) I hereby consent to participate in this study. ☐

f) I hereby give permission to undergo complete clinical examination and biochemical tests. ☐

Signature/thumb impression
Patient's Name :
Address:

<u>ஆராய்ச்சி தகவல் தாள்</u>

ஆராய்ச்சி தலைப்பு

எச்.ஐ.வி. நோயால் பாதிக்கப்பட்டு மற்றும் அதற்குரிய அதிவீரியமிக்க மருந்துகளை உட்கொள்ளும் ஆண்கள் மற்றும் பெண்களின் தைராய்டு சுரப்பியில் ஏற்படும் மாற்றங்களை அறிதல் மற்றும் தைராய்டு உந்து ஹார்மோன் மற்றும் சிடி நான்கு அளவினை ஒப்பிடுதல் பற்றிய ஆய்வு

ஆராய்ச்சியாளர் பெயர் : **பொ.கார்த்திக்**
ஆராய்ச்சி இடம் : ராஜீவ்காந்தி அரசு பொது மருத்துவமனை, சென்னை
பங்கேற்பாளர் பெயர் :
வயது :
பாலினம் :

ஆராய்ச்சியின் நோக்கம்:

எச்.ஐ.வி. நோயால் பாதிக்கப்பட்டு, அதற்குரிய வீரியமிக்க மருந்தினை உட்கொள்ளும் ஆண்கள் மற்றும் பெண்களுக்கு பல்வேறு நாளமில்லா சுரப்பியில் பிரச்சனைகள் ஏற்படலாம், அதில் தைராய்டு சுரப்பியில் ஏற்படும் குறைபாடுகளை அறிவதே இந்த ஆராய்ச்சியின் நோக்கமாகும். மற்றும் தைராய்டு உந்து ஹார்மோன் சிடி நான்கு அளவினை ஒப்பிட்டு நோயின் தீவிர தன்மையை உணர்ந்து கொள்வதுமே இந்த ஆராய்ச்சியின் நோக்கமாகும்.

ஆராய்ச்சி முறை:

இந்த ஆராய்ச்சியில் உங்கள் இரத்தத்தில் தைராய்டு சுரப்பியின் செயல்பாட்டை அறியும் பரிசோதனையும், சிடி நான்கு அளவினை அறியும் பரிசோதனையும் செய்து தகவல்களை ஆராய்வோம். இதற்காக உங்களிடமிருந்து 5மி.லி இரத்தம் மட்டும் ஒரு முறை எடுக்கப்படும் என்பதை தெரிவித்துக்கொள்கிறோம்.

ஆராய்ச்சியின் பலன் மற்றும் தீங்கு

இந்த ஆராய்ச்சியில் தைராய்டு சுரப்பியில் ஏற்படும் குறைபாடுகள் உறுதிசெய்யப்பட்டால், தைராக்ஸினை மருந்தாக பயன்படுத்தி, தைராய்டு குறைபாட்டினால் ஏற்படும் பிரச்சினைகளை நீக்க நன்மை உருவாகலாம். இந்த ஆராய்ச்சியின் மூலம் பங்கேற்பவர்களுக்கு எந்த தீங்கும் கிடையாது. நீங்களும் இந்த ஆராய்ச்சியில் பங்கேற்க நாங்கள் விரும்புகிறோம்.

முடிவுகளை அல்லது கருத்துக்களை வெளியிடும் போதோ அல்லது ஆராய்ச்சியின் போதோ தங்கள் பெயரையோ அல்லது அடையாளங்களையோ வெளியிடமாட்டோம் என்பதையும் தெரிவித்துக்கொள்கிறோம்.

இந்த சிறப்பு பரிசோதனையின் முடிவுகளை ஆராய்ச்சியின் போது அல்லது அதன் முடிவில் அறிவிக்கப்படும் என்பதையும் தெரிவித்துக்கொள்கிறோம். இதனால் தங்களது ஆய்வறிக்கையோ, அன்றாட செயல்பாடுகளோ பாதிக்கப்படாது என்று தெரிவித்துக்கொள்கிறோம்.

இந்த ஆராய்ச்சியில் பங்கேற்பது தங்களுடைய சொந்த விருப்பத்தின் பேரில் தான் இருக்கிறது. மேலும் நீங்கள் எந்த நேரமும் இந்த ஆராய்ச்சியிலிருந்து பின்வாங்கலாம் என்பதையும் தெரிவித்துக்கொள்கிறோம்.

ஆராய்ச்சியாளர் கையொப்பம் **பங்கேற்பாளர் கையொப்பம்**

நாள் : ராஜீவ்காந்தி அரசு பொது மருத்துவமனை
இடம் :

<u>ஆராய்ச்சி ஒப்புதல் தாள்</u>

ஆராய்ச்சி தலைப்பு

எச்.ஐ.வி. நோயால் பாதிக்கப்பட்டு மற்றும் அதற்குரிய அதிவீரியமிக்க மருந்துகளை உட்கொள்ளும் ஆண்கள் மற்றும் பெண்களின் தைராய்டு சுரப்பியில் ஏற்படும் மாற்றங்களை அறிதல் மற்றும் தைராய்டு உந்து ஹார்மோன் மற்றும் சிடி நான்கு அளவினை ஒப்பிடுதல் பற்றிய ஆய்வு

ஆராய்ச்சியாளர் பெயர் : **பொ.கார்த்திக்**
ஆராய்ச்சி இடம் : ராஜீவ்காந்தி அரசு பொது மருத்துவமனை, சென்னை
பங்கேற்பாளர் பெயர் :
வயது :
பாலினம் :

இந்த ஆராய்ச்சியின் விவரங்களும் அதன் நோக்கமும் முழுமையாக எனக்கு தெளிவாக விளக்கப்பட்டது.

எனக்கு விளக்கப்பட்ட விஷயங்களை புரிந்துகொண்டு நான் எனது சம்மதத்தை தெரிவிக்கிறேன்.

எனது இரத்தத்தில் தைராய்டு சுரப்பியின் செயல்பாடடை அறியும் பரிசோதனையும், சிடி நான்கு பரிசோதனையும் செய்துகொள்ள சம்மதம்.

இந்த ஆராய்ச்சியில் யாருடைய நிர்பந்தமின்றி சொந்த விருப்பத்தின் பேரில் சம்மதிக்கிறேன்.

இந்த ஆராய்ச்சியில் இருந்து நான் எந்த நேரமும் பின்வாங்கலவாம் என்றும், அதனால் எந்த பாதிப்பும் ஏற்படாது என்பதையும் புரிந்து கொண்டேன்.

நான் இந்த ஆராய்ச்சியின் விவரங்களை கொண்ட தகவல்களை பெற்றுக்கொண்டேன்.

இந்த பரிசோதனைக்கு எனது உடலில் இருந்து ஊசி மூலம் 5 மி.லி இரத்தம் ஒரு முறை மட்டும் எடுக்க சம்மதிக்கிறேன். இரத்தம் எடுக்கும் போது, வலி, மயக்கம் போன்ற பின்விளைவுகள் ஏற்படலாம் என்றும் தெரிந்து கொண்டேன்.

நான் என்னுடைய சுய நினைவுடன் மற்றும் முழு சுதந்திரத்துடன் இந்த ஆராய்ச்சிக்கு என்னை பரிசோதிக்க சம்மதிக்கிறேன்.

ஆராய்ச்சியாளர் கையொப்பம் **பங்கேற்பாளர் கையொப்பம்**

நாள் : ராஜீவ்காந்தி அரசு பொது மருத்துவமனை
இடம் :

INTRODUCTION

HIV [human immune defi ency virus] the etiological agent of AIDS. Two types HIV virus HIV 1 and HIV 2 which causes cytopathic effects either directly or indirectly .

The various spectrum of endocrine dysfunctions manifested in patients with HIV are related directly to virus or secondary to opportunistic infections, drugs, malignancy and mainly affects ADRENAL GLAND, GONADS, THYROID, PITUTARY.

THYROID DYSFUNCTION is a recognized entity in HIV infection.

Thyroid function alteration seen in up to 10 to 15% of HIV patients.

The predominant abnormality is sub clinical hypothyroidism but both

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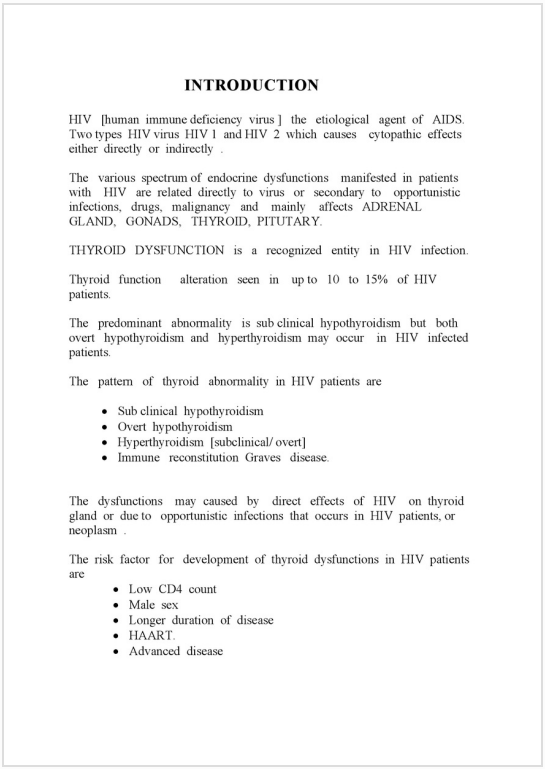

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The predominant abnormality is sub clinical hypothyroidism but both overt hypothyroidism and hyperthyroidism may occur in HIV infected patients.

The pattern of thyroid abnormality in HIV patients are

- Sub clinical hypothyroidism
- Overt hypothyroidism
- Hyperthyroidism [subclinical/ overt]
- Immune reconstitution Graves disease.

The dysfunctions may caused by direct effects of HIV on thyroid gland or due to opportunistic infections that occurs in HIV patients, or neoplasm .

The risk factor for development of thyroid dysfunctions in HIV patients are

- Low CD4 count
- Male sex
- Longer duration of disease
- HAART.
- Advanced disease